VOLUME 52 NUMBER 5 MAY 1959

PROCEEDINGS
of the
ROYAL
SOCIETY OF MEDICINE

Published by
THE ROYAL SOCIETY OF MEDICINE, 1 WIMPOLE STREET, LONDON, W.1

All rights reserved

In all types of insomnia, CARBRITAL* secures a full night's refreshing sleep, with a fresh awakening on the morrow. Rapid onset of sleep is obtained by incorporating in the CARBRITAL formula a moderate dose of the quick-acting hypnotic, pentobarbitone sodium. This action is prolonged by the use of carbromal, a milder long-acting sedative, which maintains sleep for up to eight hours, leaving the patient with the minimum of depression on awakening.

IN ALL TYPES OF INSOMNIA

quick action

prolonged sedation

minimal after-effects

CARBRITAL

*Trade Mark

Capsules: In bottles of 25 and 250 capsules, each containing pentobarbitone sodium (1½ grs.) and carbromal (4 grs.)
Elixir: in bottles of 4, 16 and 80 fl. ozs. Each fluid drachm (one teaspoonful) represents pentobarbitone sodium (¼ gr.) and carbromal (⅔ gr.)

PARKE, DAVIS & CO. LTD. (*Inc. USA*), Hounslow, Middlesex. Tel: Hounslow 2361

VOLUME 52 NUMBER 5 MAY 1959

PROCEEDINGS

of the

ROYAL SOCIETY OF MEDICINE

ISSUED UNDER THE DIRECTION OF THE EDITORIAL COMMITTEE

HONORARY EDITORS

E. C. WARNER SELWYN TAYLOR

EDITORIAL REPRESENTATIVES OF SECTIONS

O. P. DINNICK (Anæsthetics)
RICHARD ASHER (Clinical)
M. CRAWFORD (Comparative Medicine)
D. I. WILLIAMS (Dermatology)
N. F. MACLAGAN (Endocrinology)
J. C. McDONALD (Epidem. and Preventive Med.)
A. C. WHITE (Exper. Med. & Therap.)
L. CARLYLE LYON (General Practice)
Sir ZACHARY COPE (History of Medicine)
F. C. W. CAPPS (Laryngology)
PHILIP ELLMAN (Medicine)
MACDONALD CRITCHLEY (Neurology)
W. C. W. NIXON (Obstetrics and Gynæcology)
J. H. HOVELL (Odontology)
S. J. H. MILLER (Ophthalmology)
T. J. FAIRBANK (Orthopædics)
G. H. BATEMAN (Otology)
D. MacCARTHY (Pædiatrics)
B. W. LACEY (Pathology)
A. C. BOYLE (Physical Medicine
HAROLD DODD (Proctology)
J. S. PIPPARD (Psychiatry)
A. M. RACKOW (Radiology)
D. H. PATEY (Surgery)
Surg. Cdr. F. P. ELLIS (United Services)
A. CLIFFORD MORSON (Urology)

SECRETARY OF THE ROYAL SOCIETY OF MEDICINE

R. T. HEWITT

All correspondence to

THE HONORARY EDITORS, 1, WIMPOLE STREET, LONDON, W.1

(Tel.: LANgham 2070)

Distributing Agents:

H. K. LEWIS & CO. LTD., 136 GOWER STREET LONDON, W.C.1

In the U.S.A.:

GRUNE & STRATTON, INC., 381 FOURTH AVENUE, NEW YORK 16

Advertisement Managers:

H. S. JANES & PARTNERS LTD., 99 GOWER STREET, LONDON, W.C.1

Telephone: EUSton 3221

Monthly, 10s. 6d. net. Annual Subscription, £6 6s. in the British Commonwealth, $19.00 in the U.S.A.

In all types of insomnia, CARBRITAL* secures a full night's refreshing sleep, with a fresh awakening on the morrow. Rapid onset of sleep is obtained by incorporating in the CARBRITAL formula a moderate dose of the quick-acting hypnotic, pentobarbitone sodium. This action is prolonged by the use of carbromal, a milder long-acting sedative, which maintains sleep for up to eight hours, leaving the patient with the minimum of depression on awakening.

IN ALL TYPES OF INSOMNIA

quick action

prolonged sedation

minimal after-effects

CARBRITAL

*Trade Mark

Capsules: In bottles of 25 and 250 capsules, each containing pentobarbitone sodium (1½ grs.) and carbromal (4 grs.)
Elixir: in bottles of 4, 16 and 80 fl. ozs. Each fluid drachm (one teaspoonful) represents pentobarbitone sodium (¼ gr.) and carbromal (⅔ gr.)

PARKE, DAVIS & CO. LTD. (*Inc. USA*), Hounslow, Middlesex. Tel: Hounslow 2361

VOLUME 52 NUMBER 5 MAY 1959

PROCEEDINGS

of the

ROYAL SOCIETY OF MEDICINE

ISSUED UNDER THE DIRECTION OF THE EDITORIAL COMMITTEE

HONORARY EDITORS

E. C. WARNER SELWYN TAYLOR

EDITORIAL REPRESENTATIVES OF SECTIONS

O. P. DINNICK (Anæsthetics)
RICHARD ASHER (Clinical)
M. CRAWFORD (Comparative Medicine)
D. I. WILLIAMS (Dermatology)
N. F. MACLAGAN (Endocrinology)
J. C. McDONALD (Epidem. and Preventive Med.)
A. C. WHITE (Exper. Med. & Therap.)
L. CARLYLE LYON (General Practice)
Sir ZACHARY COPE (History of Medicine)
F. C. W. CAPPS (Laryngology)
PHILIP ELLMAN (Medicine)
MACDONALD CRITCHLEY (Neurology)
W. C. W. NIXON (Obstetrics and Gynæcology)
J. H. HOVELL (Odontology)
S. J. H. MILLER (Ophthalmology)
T. J. FAIRBANK (Orthopædics)
G. H. BATEMAN (Otology)
D. MacCARTHY (Pædiatrics)
B. W. LACEY (Pathology)
A. C. BOYLE (Physical Medicine
HAROLD DODD (Proctology)
J. S. PIPPARD (Psychiatry)
A. M. RACKOW (Radiology)
D. H. PATEY (Surgery)
Surg. Cdr. F. P. ELLIS (United Services)
A. CLIFFORD MORSON (Urology)

SECRETARY OF THE ROYAL SOCIETY OF MEDICINE

R. T. HEWITT

All correspondence to

THE HONORARY EDITORS, 1, WIMPOLE STREET, LONDON, W.1

(Tel.: LANgham 2070)

Distributing Agents:

H. K. LEWIS & CO. LTD., 136 GOWER STREET LONDON, W.C.1

In the U.S.A.:

GRUNE & STRATTON, INC., 381 FOURTH AVENUE, NEW YORK 16

Advertisement Managers:

H. S. JANES & PARTNERS LTD., 99 GOWER STREET, LONDON, W.C.1

Telephone: EUSton 3221

Monthly, 10s. 6d. net. Annual Subscription, £6 6s. in the British Commonwealth, $19.00 in the U.S.A.

In all types of insomnia, CARBRITAL* secures a full night's refreshing sleep, with a fresh awakening on the morrow. Rapid onset of sleep is obtained by incorporating in the CARBRITAL formula a moderate dose of the quick-acting hypnotic, pentobarbitone sodium. This action is prolonged by the use of carbromal, a milder long-acting sedative, which maintains sleep for up to eight hours, leaving the patient with the minimum of depression on awakening.

IN ALL TYPES OF INSOMNIA

quick action

prolonged sedation

minimal after-effects

CARBRITAL

*Trade Mark

Capsules: In bottles of 25 and 250 capsules, each containing pentobarbitone sodium (1½ grs.) and carbromal (4 grs.)
Elixir: in bottles of 4, 16 and 80 fl. ozs. Each fluid drachm (one teaspoonful) represents pentobarbitone sodium (¼ gr.) and carbromal (¾ gr.)

PARKE, DAVIS & CO. LTD. (*Inc. USA*), Hounslow, Middlesex. Tel: Hounslow 2361

VOLUME 52 NUMBER 5 MAY 1959

PROCEEDINGS

of the

ROYAL SOCIETY OF MEDICINE

ISSUED UNDER THE DIRECTION OF THE EDITORIAL COMMITTEE

HONORARY EDITORS

E. C. WARNER SELWYN TAYLOR

EDITORIAL REPRESENTATIVES OF SECTIONS

O. P. DINNICK (Anæsthetics)
RICHARD ASHER (Clinical)
M. CRAWFORD (Comparative Medicine)
D. I. WILLIAMS (Dermatology)
N. F. MACLAGAN (Endocrinology)
J. C. McDONALD (Epidem. and Preventive Med.)
A. C. WHITE (Exper. Med. & Therap.)
L. CARLYLE LYON (General Practice)
Sir ZACHARY COPE (History of Medicine)
F. C. W. CAPPS (Laryngology)
PHILIP ELLMAN (Medicine)
MACDONALD CRITCHLEY (Neurology)
W. C. W. NIXON (Obstetrics and Gynæcology)
J. H. HOVELL (Odontology)
S. J. H. MILLER (Ophthalmology)
T. J. FAIRBANK (Orthopædics)
G. H. BATEMAN (Otology)
D. MacCARTHY (Pædiatrics)
B. W. LACEY (Pathology)
A. C. BOYLE (Physical Medicine
HAROLD DODD (Proctology)
J. S. PIPPARD (Psychiatry)
A. M. RACKOW (Radiology)
D. H. PATEY (Surgery)
Surg. Cdr. F. P. ELLIS (United Services)
A. CLIFFORD MORSON (Urology)

SECRETARY OF THE ROYAL SOCIETY OF MEDICINE

R. T. HEWITT

All correspondence to

THE HONORARY EDITORS, 1, WIMPOLE STREET, LONDON, W.1

(Tel.: LANgham 2070)

Distributing Agents:

H. K. LEWIS & CO. LTD., 136 GOWER STREET LONDON, W.C.1

In the U.S.A.:

GRUNE & STRATTON, INC., 381 FOURTH AVENUE, NEW YORK 16

Advertisement Managers:

H. S. JANES & PARTNERS LTD., 99 GOWER STREET, LONDON, W.C.1

Telephone: EUSton 3221

Monthly, 10s. 6d. net. Annual Subscription, £6 6s. in the British Commonwealth, $19.00 in the U.S.A.

PRECORTISYL

PREDNISOLONE

SKIN LOTION:
solution of prednisolone in a spray bottle

Quick and easy application

Economical:
wide application with minimal quantity

'No-touch' application:
avoidance of pain, and possible infection from finger spreading

SKIN CREAM:
a vanishing cream of soluble prednisolone in a water-miscible vehicle

PACKINGS

PreCortisyl Skin Lotion : 0.25% prednisolone in 20 ml. plastic spray bottle

PreCortisyl Skin Cream : 0.25% and 0.5% prednisolone. Tubes of 5 and 15 G.

ROUSSEL
LONDON, N.W.10
LADbroke 6611

LS/77

PROCEEDINGS

of the

ROYAL SOCIETY OF MEDICINE

Vol. 52 No. 5 May 1959

CONTENTS

Whole Proceedings Page

Section of Pathology

Cellular Associations in Normal and Abnormal Lymphocytes (Illustrated by a Film).—President's Address by Professor R. J. V. PULVERTAFT, O.B.E., M.D., F.R.C.P. 315

Section of Anæsthetics

An Evaluation of General Anæsthetic Techniques for Use in the Dental Surgery.—W. S. MCCONNELL, M.B., F.F.A. R.C.S. 323

Section of Radiology

October 17, 1958

Some Radiological Aspects of Congenital Anomalies of the Spine in Childhood and Infancy.—JOHN FAWCITT, M.R.C.S., L.R.C.P., D.M.R.(D.) 331

Observations on Spinal Tumours in Childhood [*Abridged*].—KENNETH TILL, F.R.C.S. 333

November 21, 1958

DISCUSSION ON TESTICULAR TUMOURS 336

A Technical Advance in Irradiation Technique.—ANTHONY GREEN, F.R.C.S., F.F.R. 344

Section of Experimental Medicine and Therapeutics

SYMPOSIUM ON SOME NEW APPROACHES TO CALCIUM METABOLISM 347

Books Recently Presented and Placed in the Society's Library. Books Received for Review 354

Section of Orthopædics

The Surgery of the Hip.—President's Address by J. S. BATCHELOR, F.R.C.S. 355

Section of the History of Medicine

Strafford—the Medical Background.—A. LESLIE BANKS, M.A., M.D., F.R.C.P., D.P.H. .. 361

Section of Dermatology

November 20, 1958 (contd.)

Erythema Gyratum Repens (Gammel, 1952).—J. SCHNEEWEISS, M.B. (for S. C. GOLD, M.D., F.R.C.P.) 367

Alopecia Mucinosa (Pinkus).—C. J. STEVENSON, M.D. 368

List of other Cases shown 370

December 18, 1958

Indeterminate Leprosy.—W. H. JOPLING, M.R.C.P., D.T.M.&H. 370

Unusually Widespread Tinea Corporis.—C. M. RIDLEY, M.R.C.P. 371

List of other Cases shown 372

Section of Comparative Medicine

Spontaneous Gastric Dilatation in Man.—D. E. BOLT, F.R.C.S. 373

Physiological Effects of Distension of the Rumen and Œsophagus in Ruminants.—R. N. B. KAY, M.A., Ph.D., and A. T. PHILLIPSON, Ph.D., M.R.C.V.S. 374

Bloat in Cattle. Aspects of Research Work at Plant Chemistry Division, D.S.I.R., Palmerston North, New Zealand.—J. L. MANGAN, M.Sc., Ph.D. 376

Acute Gastric Distension in Man and Animals.—NORMAN C. TANNER, F.R.C.S. 379

Continued overleaf

CONTENTS (*continued*)

	Whole Proceedings Page
Section of Pædiatrics	
December 10, 1958	
Going to Hospital with Mother. A Documentary Film.—JAMES ROBERTSON	381
February 27, 1959	
DISCUSSION (*By Title*)	384
Section of Proctology	
Intra-abdominal Repair of Rectal Prolapse in Women.—E. C. B. BUTLER, F.R.C.S.	385
New Operative Procedure for Complete Prolapse of the Rectum [*Summary*].—D. W. BRACEY, Ch.M.	387
The Development of Carcinoma of the Large Intestine in Ulcerative Colitis [*Summary*].—I. M. P. DAWSON, M.D., M.R.C.P., and J. PRYSE-DAVIES, M.B.	387
Congenital Rectal Prolapse.—TOM ROWNTREE, M.Chir., M.S., F.R.C.S.	388
Primary Pruritus Ani.—F. AUSTIN HENLEY, F.R.C.S.	390
Book Reviews	391

N.B.—The Society does not hold itself in any way responsible for the statements made or the views put forward in the various papers.

Copyright: The Society holds the copyright of all matter accepted for publication in the *Proceedings*. Requests for subsequent publication elsewhere should be made to the Honorary Editors, Royal Society of Medicine . . . . The copyright of all papers presented at meetings by Fellows of the Society or Members of the Sections (other than those which have been previously published) shall be deemed to be the property of the Society until a decision has been made by the Society in regard to their publication.

In light diets . . .

In light diets, as well as under more normal regimes, Lucozade fulfils a most valuable role, not only in abating thirst and protecting the mucosa of the mouth, but also in arousing the appetite and contributing to the retention of more solid food. Lucozade is especially useful in the diet of patients in whom nausea of pregnancy, dehydration, or other special conditions make it necessary to supply an easily tolerated, nutritious fluid intake.

Lucozade is lightly carbonated with an attractive golden colour and a pleasant citrus flavour. It contains 23.5% w/v Liquid Glucose and its energy value is 21 Calories per fluid ounce. It is supplied in 6 oz. and 26 oz. bottles.

LUCOZADE

Baillière Tindall & Cox

A MODERN PRACTICE OF OBSTETRICS
by **D. M. Stern**, M.A., M.B., B.Ch., F.R.C.S., F.R.C.O.G., and **C. W. F. Burnett**, M.D., F.R.C.S., F.R.C.O.G.
Second Edition. 268 pages. 140 illustrations. **45s.** Postage 2s. 3d.

ATOMIC MEDICINE
Edited by **C. F. Behrens**, M.D., F.A.C.R., assisted by 24 other contributors.
Third Edition. 720 pages. 145 illustrations. **120s.** Postage 2s. 9d.

CARDIOVASCULAR SOUND IN HEALTH AND DISEASE
by **Victor A. McKusick**, M.D.
580 pages. 494 illustrations. **120s.** Postage 2s. 9d.

HERMAPHRODITISM, GENITAL ANOMALIES AND RELATED ENDOCRINE DISORDERS
by **H. W. Jones, Jr.** M.D., and **W. W. Scott**, M.D., Ph.D.
472 pages. 466 illustrations. **128s.** Postage 2s. 9d.

REVERSIBLE RENAL INSUFFICIENCY
DIAGNOSIS AND TREATMENT
by **D. H. Atlas**, M.D., Ph.D., F.A.C.P., and **P. Gaberman**, M.D.
242 pages. 19 illustrations. **56s.** Postage 2s. 6d.

7 & 8 HENRIETTA STREET, LONDON W.C.2

New Books and New Editions

January to June 1959

LEPROSY
In Theory and Practice
Edited by R. G. COCHRANE. 84s., post 2s.

A SYNOPSIS OF OBSTETRICS AND GYNÆCOLOGY
12th Edition
By ALECK W. BOURNE. 35s., post 1s. 3d.

A MANUAL OF ANÆSTHETIC TECHNIQUES
2nd Edition
By W. J. PRYOR. 27s. 6d., post 1s. 1d.

A SYNOPSIS OF ANÆSTHESIA
4th Edition
By J. ALFRED LEE. 27s. 6d., post 1s. 3d.

NOTES ON INJECTIONS FOR NURSES
By T. H. WHITE. 2s. 6d., post 2d.

SMALLPOX
Variations on a Theme by Sydenham.
By PAUL WILKINSON. 17s. 6d.

A SYNOPSIS OF SKIN DISEASES
By BETHEL SOLOMONS, Jun. 30s., post 10d.

A SYNOPSIS OF BIOLOGY
By W. B. CROW. 90s.

ELEMENTARY MEDICAL THERAPEUTICS
By G. F. WALKER. 7s. 6d.

THE MODERN TREATMENT OF ASTHMA
With Special Reference to Gold Therapy
2nd Edition
By L. BANSZKY. About 21s.

THE CLINICAL APPRENTICE
2nd Edition
By JOHN M. NAISH and JOHN APLEY. About 12s. 6d.

THE MEDICAL ANNUAL 1959
Edited by R. MILNES WALKER and R. BODLEY SCOTT.
Pre-publication price 38s. 6d., post free.
After publication 42s., plus postage.

Illustrated catalogue available on request.

John Wright & Sons Ltd., Bristol

Oxford University Press

A Clinical Introduction to Heart Disease

CRIGHTON BRAMWELL *Emeritus Professor of Cardiology in the University of Manchester*

This book has been written specially for general practitioners and senior students who intend to enter general practice. No attempt has been made to cover the whole field of cardiology: instead Professor Bramwell has paid particular attention to those problems in which—based on his own wide experience—the general practitioner most needs help. His aim throughout has been to discuss the diagnosis, treatment, and prognosis of patients with heart disease in their own homes, by their own family doctor, and nearly all the methods given can be carried out without special equipment or hospital facilities. A valuable feature is the series of case histories —fully illustrated by x-rays and electrocardiographic tracings—that accompany nearly every condition described.

238 pages 62 illustrations 21s. net

Major Endocrine Disorders

S. LEONARD SIMPSON *Consultant Endocrinologist, St. Mary's Hospital*

THIRD EDITION with the collaboration of

A. STUART MASON, *Consultant Endocrinologist, The London Hospital*
G. I. M. SWYER, *Consultant Endocrinologist, Department of Obstetrics and Gynæcology, University College Hospital*

The text of this third edition has been very thoroughly revised and much of it has been rewritten. It gives a straightforward, comprehensive yet concise account of all major endocrine disorders that are likely to be encountered by consultant physicians and general practitioners during their normal clinical work and it covers fully all problems that may arise concerning diagnosis, prognosis, and treatment. The clinical accounts are prefaced by an introductory section, for each endocrine gland in turn, giving all relevant information on the physiology and chemistry of the gland. This will enable both the methods and the interpretation of modern laboratory investigations and hormone assays to be readily understood and therefore capable of being used as valuable aids to clinical judgement.

468 pages 55 illustrations 50s. net

Oxford University Press

Sympathectomy

P. A. G. MONRO *Lecturer in Anatomy in the University of Cambridge*

This monograph describes in detail the lumbar sympathetic ganglia and the work leading to their discovery—first published in a paper written jointly by the author and Professor J. D. Boyd—and it provides detailed information on the part they play in the retention of autonomic function after sympathectomy.

It is based on continued observation of more than fifty patients for periods up to five years, many of whom are still attending for re-examination. It also contains a detailed account of *post mortem* findings and histological examinations, which are discussed in relation to the retention of autonomic activity after sympathectomy, and it explains why it is retained in certain areas of the body after appropriate sympathectomy.

290 pages 84 illustrations 75s. net

An Introduction to Medical Genetics

J. A. FRASER ROBERTS *Director, Clinical Genetics Research Unit, Medical Research Council*

SECOND EDITION

The text of this new edition has been completely rewritten but the general plan remains the same as in the first edition. It is addressed primarily to clinicians and senior students, its aim being to give guidance during the clinical and postgraduate years in the application of genetics to the practical problems of the causation of abnormality and disease. Previous knowledge of genetics is not taken for granted; the basic principles are restated fully, and on this foundation is built up, not a recapitulation of the science of genetics, but an exposition of the applied science of *medical* genetics, dealing with the human subject as observed in the community, in general medical practice, and in hospital.

284 pages 107 illustrations (June) 35s. net

THE PATHOLOGY OF TUMOURS OF THE NERVOUS SYSTEM

PROFESSOR DOROTHY RUSSELL AND L. J. RUBINSTEIN

A companion to Neuropathology by Greenfield, published in April 1958, which has already become a standard work. To be published in May 70s. net

HERNIA

Sir HENEAGE OGILVIE, K.B.E., F.R.C.S.

A critical account of the various operations for hernia with clear instructions on diagnosis and treatment based on the lifetime's experience of a world authority. 28s. net.

A PRACTICE OF THORACIC SURGERY

Second Edition

A. L. D'ABREU, O.B.E., Ch.M., F.R.C.S.

"This new edition is a worthy successor of the former and the author has been able to bring the text completely up to date."—*British Journal of Surgery.* 100s. net.

THE PATHOLOGY AND MANAGEMENT OF PORTAL HYPERTENSION

R. MILNES WALKER, M.S., F.R.C.S.

An account of venous shunting operations to serve as a guide to clinicians who have to treat these cases. 35s. net.

ORTHOPÆDIC SURGERY *Fifth Edition*

Sir WALTER MERCER, F.R.C.S.

The new edition has been completely revised to take account of the many changes in the subject. 80s. net.

DISEASES OF CHILDREN IN THE SUBTROPICS AND TROPICS

H. C. TROWELL, O.B.E., M.D., F.R.C.P., and D. B. JELLIFFE, M.D., M.R.C.P., D.C.H.

"The authors and the Editors are to be congratulated, as well as the publishers upon the production of a volume which not only fills a gap in medical literature but fills it entirely adequately."—*East African Medical Journal.*
"It can be strongly recommended for all working in preventive or curative pediatrics in the subtropics and tropics."—*J. Tropical Pædiatrics.* 105s. net.

POLIOMYELITIS

W. RITCHIE RUSSELL

"It would be hard to find anywhere an account of the clinical aspects of poliomyelitis so concise and yet so comprehensive."—*The Lancet.* 16s. net.

EDWARD ARNOLD (PUBLISHERS) LTD.

41 Maddox Street, London, W.1

ST. ANDREW'S HOSPITAL

FOR NERVOUS AND MENTAL DISEASES

NORTHAMPTON

President—THE EARL SPENCER

Medical Superintendent—THOMAS TENNENT, M.D., F.R.C.P., D.P.H., D.P.M.

THIS Registered Hospital is situated in 130 acres of park and pleasure grounds. Voluntary patients, who are suffering from incipient mental disorders or who wish to prevent recurrent attacks of mental trouble, temporary patients and certified patients of both sexes are received for treatment. Careful clinical, biochemical, bacteriological and pathological examinations. Private rooms with special nurses, male or female, in the Hospital or in one of the numerous villas in the grounds of the various branches, can be provided.

WANTAGE HOUSE

This is a Reception Hospital in detached grounds with a separate entrance, to which patients can be admitted. It is equipped with all the apparatus for the complete investigation and treatment of Mental and Nervous Disorders by the most modern methods: insulin treatment is available for suitable cases. It contains special departments for Hydrotherapy by various methods, including Turkish and Russian Baths, the prolonged immersion bath, Vichy Douche, Scotch Douche, Electrical baths, Plombiere's treatment, etc. There is an Operating Theatre, a Dental Surgery, an X-ray Room, an Ultra-Violet Apparatus and a Department for Diathermy and High-Frequency treatment. It also contains Laboratories for Biochemical, Bacteriological and Pathological Research. Psycho-therapeutic treatment is employed when indicated.

MOULTON PARK

Two miles from the main Hospital there are several branch establishments and villas situated in a park and farm of 650 acres. Milk, meat, fruit and vegetables are supplied to the Hospital from the farm, gardens and orchards of Moulton Park. Occupational Therapy is a feature of this Branch, and patients are given every facility for occupying themselves in farming, gardening and fruit growing.

BRYN-Y-NEUADD HALL

The seaside house of St. Andrew's Hospital is beautifully situated in a park of 330 acres, at Llanfairfechan, amidst the finest scenery in North Wales. On the north-west side of the Estate a mile of sea-coast forms the boundary. Patients may visit this branch for a short seaside change or for longer periods. The Hospital has its own private bathing house on the seashore. There is trout-fishing in the park.

At all the branches of the Hospital there are cricket grounds, football and hockey grounds, lawn tennis courts (grass and hard courts), croquet grounds, golf courses, and bowling greens. Ladies and gentlemen have their own gardens, and facilities are provided for handicrafts, such as carpentry, etc.

For terms and further particulars apply to the Medical Superintendent: TELEPHONE No. 4354 Northampton (three lines) who can be seen in London by appointment.

Have you had your copy?

Authoritative Information

Compiled by the discoverers of chlorothiazide

Copies of this comprehensive booklet describing therapy with 'Saluric' will gladly be supplied upon request

SALURIC

Regd.

(CHLOROTHIAZIDE)

the oral diuretic with additional hypotensive properties

MSD MERCK SHARP & DOHME LIMITED, HODDESDON, HERTS.

0.5 G. 'Saluric' tablets are available in bottles of 100 and 500.

RIKER

You can treat iron deficiency anaemia better if you prescribe

FERROIDS

Virtually fulfils the requirements for the ideal haematinic. High utilization of iron. Exceptional freedom from side effects

Each golden yellow tablet contains 350 mg. of iron aminoates. This interesting new compound is produced by chelating iron with amino acids. The presence of amino acids profoundly affects the absorption of iron and they are responsible for the unique properties of 'Ferroids'.

DOSE 1 TO 2 TABLETS THREE TO FOUR TIMES A DAY.

Treatment with 'Ferroids' is relatively inexpensive. The basic N.H.S. cost of 1 week's treatment is 1/2 to 3/1, based on the large pack of 1,000.

FORMULA

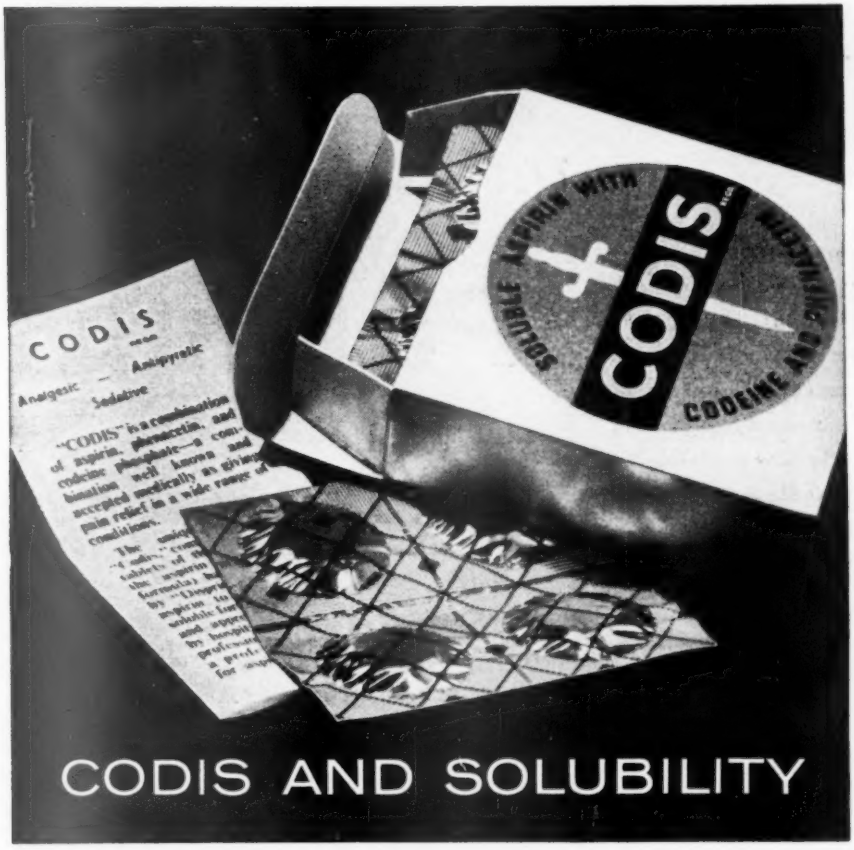
Each tablet contains:
Iron aminoates 350 mg.
(corresponding to 35 mg. elemental iron)
Aneurine hydrochloride 1 mg.

PACKS AND BASIC N·H·S PRICES

100's 6/8d
1,000's 54/8d

Exempt from Purchase Tax

'FERROIDS' is a registered trade mark of
RIKER LABORATORIES LIMITED • LOUGHBOROUGH • LEICS.



THE GREAT ADVANTAGE of Codis is that it provides a codeine compound tablet in which the aspirin content is soluble in water. (The codeine constituent is also soluble, and the phenacetin is in very fine suspension.)

This is achieved by careful compounding and preparation, resulting in tablets which are quickly absorbed and well tolerated—even in cases of proven intolerance to ordinary (insoluble) aspirin.

To ensure stability and easy identification, the tablets are wrapped in moisture-proof distinctive gold foils of 10 tablets each (dispensing size), or boxes containing five foils of 4 tablets each (public size).

CODIS REGD. **AVAILABLE FOR DISPENSING**

Not advertised to the public

Composition. *Each Codis tablet contains: Acid. Acetylsalicyl. B.P. 4 gr., Phenacet. B.P. 4 gr., Codein. Phosph. B.P. 0.125 gr., Calc. Carb. B.P. 1.2 gr., Acid. Cit. B.P. (exsic.) 0.4 gr.*

For clinical samples and literature, please write to Reckitt & Sons Ltd., Pharmaceutical Dept., Hull

FOR THE MANAGEMENT OF *intractable pain*

New to Great Britain, but in wide use on the continent, PALFIUM was isolated after intensive screening of hundreds of compounds and is now available to the medical profession.

Palfium*

(M.C.P.875)

ADVANTAGES

Acts swiftly and effectively without clouding consciousness or reducing mental activity.
Equally effective by oral or parenteral route.
Does not cause constipation or diarrhoea.
Minimal risk of tolerance or addiction.
Extremely low chronic toxicity.

INDICATIONS

Severe pain of inoperable carcinoma, severe colic and other forms of intractable pain.

PRESENTATION

Tablets : 5 mg. in packs of 25 and 100
Ampoules : 5 mg. in packs of 10 and 100
10 mg. in packs of 10 and 100

* d-3-methyl-2,2-diphenyl-4-morpholinobutyrylpyrrolidine (Dextromoramide)

If you have not yet obtained your copy of the booklet describing PALFIUM write to Dept. R.S.M.2

M.C.P. Pure Drugs Ltd

STATION WHARF, ALPERTON, MIDDLESEX

CHELATED IRON IN ANÆMIA OF PREGNANCY

Report on 51 patients

'Oral iron therapy will correct most of these anæmias but many preparations are not well tolerated . . . . . It would appear that ferrous aminoacetosulphate ('plesmet') is rapidly absorbed and almost free from gastrointestinal disturbance in pregnant women.'

Practitioner 1958, **181**, 731-5.

In the trial referred to above, excellent responses were obtained with PLESMET—the Ferrous aminoacetosulphate 'chelate' complex which minimizes oxidation and ensures maximum assimilation with a high degree of toleration.

Attention was also drawn to the low prescription cost and effective haemoglobin levels reached in the early weeks of treatment, the latter being better than the results obtained in pregnancy with other iron compounds.

Plesmet

Syrup—Palatable blackcurrant flavour without 'iron' taste, each teaspoonful equivalent to 25 mg. Ferrous Iron with 1 mg. Aneurine Hydrochloride B.P.

2 oz. bottles — 2/-
40 oz. bottles — 18/-

Basic N.H.S. Price

Tablets—Each equivalent to 50 mg. Ferrous Iron with 1 mg. Aneurine Hydrochloride B.P.

Bottles of 100 — 2/8
Bottles of 1000 — 17/6

C&C LTD. REGD. TRADE MARK

COATES & COOPER LTD.

PYRAMID WORKS • WEST DRAYTON • MIDDLESEX

. . . for hygienic

BLANKET WASHING

in Hospitals

Infection from bedclothes has always been an item of concern in Hospitals. Until recently the most satisfactory method was to wash the blankets in a suitable detergent, rinse and then treat with a cation-active germicide. The action of cleaning and disinfection can now be carried out *simultaneously* by using the new detergent/sterilizer Hytox, which is effective against a wide range of Gram-positive and Gram-negative organisms.

Extract from letter to "The Lancet" 11.10.58

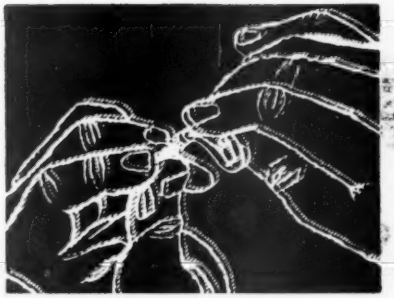
. . . Hytox has now been tried at one of our Hospitals with great success. The blankets emerged very white, soft and clean and the fibres have anti-bacterial properties and are sterile. Hytox is also inactivated by traces of ordinary washing soap in the blanket or in the crevices of the washing machine; so the first time a used blanket is washed the results may be disappointing. However, the second time the blankets are washed in a clean machine the results are very satisfactory.

HYTOX

THE COMBINED DETERGENT/STERILIZER

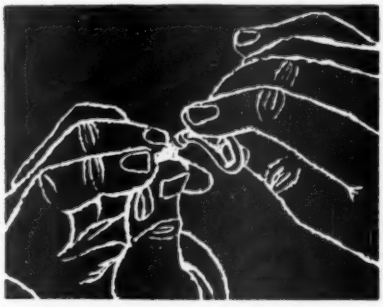
Write for literature and testing sample to:

DOMESTOS LTD. *Consultants in Hygiene* NEWCASTLE UPON TYNE.



effective symptomatic relief

PARKINSON'S SYNDROME



'COGENTIN' is recommended for use in the symptomatic and palliative treatment of all aetiological groups of Parkinson's syndrome—arteriosclerotic, post-encephalitic, or idiopathic. It is mainly effective in relieving parkinsonian tremor and rigidity and in ameliorating associated symptoms such as sialorrhoea, drooling, mask-like facies, oculogyric crises, speech and writing difficulties, dysphagia, gait disturbances, and pain and insomnia due to cramps and muscle spasm. It may be given alone or in conjunction with other drugs.

Particularly effective in the relief of tremor and rigidity
Remarkably free from side-effects

Adequate daily dosage ranges from 0.5 mg. to 2 mg. in most instances.

'COGENTIN' is supplied in bottles of 100 quarter-scored tablets, each tablet containing 2 mg. of benztropine methanesulphonate.

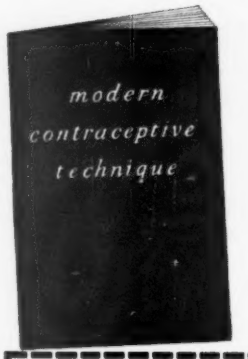
Literature will gladly be supplied at your request

COGENTIN REGD.

TABLETS BENZTROPINE METHANESULPHONATE

Made in England by:
MERCK SHARP & DOHME LIMITED · HODDESDON · HERTS

MSD



A practical reference manual on contraception

available free to all doctors

The Report of the Royal Commission on Population (1949) states:

> *"... there is nothing inherently wrong in the use of mechanical methods of contraception... public policy should be based on acceptance of voluntary parenthood and contraception."*

These words give authoritative support to the use of conception control methods as a means of planning the size of the family.

MODERN CONTRACEPTIVE TECHNIQUE presents a concise and compact survey of methods commonly used. There are notes on methods which have medical approval, and also on others which are medically contra-indicated.

TO GET YOUR COPY
write "Modern Contraceptive Technique" and "Planned Families" on your letterhead and post it to the address below.

For the use of patients
PLANNED FAMILIES explains contraceptive techniques in non-technical terms. Any number of copies will be supplied to doctors for distribution to their patients.

LONDON RUBBER CO. LTD., Department 308, HALL LANE, LONDON, E.4

RIDDOSEDD TABLETS

A Compound of SODIUM-DIETHYLBARBITURATE-PHENACETIN-CODEINE The ideal HYPNOTIC, SEDATIVE, SOPORIFIC and ANALGESIC

- **RIDDOSEDD** induces a calm, natural sleep of several hours without any resulting somnolence.
- **RIDDOSEDD** has no injurious effects upon the heart, circulation, kidneys or respiration.
- **RIDDOSEDD** is timed to set in when patients awake during the early hours of the morning, thus ensuring a continuation of normal sleep.
- **RIDDOSEDD** as a soporific is 20 times greater than that of Sodium Diethylbarbiturate.
- **RIDDOSEDD** has proved to be a most reliable and best tolerated soporific and sedative for more than twenty years.

PACKED IN BOTTLES OF 20 and 100
Please write for details to:—

Sole Manufacturers:

RIDDELL PRODUCTS LIMITED

RIDDELL HOUSE, 10-14 DUNBRIDGE STREET, LONDON, E.2
Telephone: SHOreditch 7254. Telegrams: Pneumostat, Beth, London

BRANCH OFFICE: 11 Mansfield Chambers, St. Ann's Square, Manchester 2

An analgesic cream for the treatment of neuromuscular pain

This analgesic cream is very effective in the treatment of fibrositis, muscular pain, lumbago, neuritis, neuralgia and sciatica. Free from objectionable odour, it is formulated to produce a readily absorbed cream, and helps to give rapid relief from pain.

The presence of Methyl Nicotinate produces dilation of the surface blood vessels and allows penetration of the analgesics Glycol Salicylate and Benzocaine.

FORMULA

Benzocaine B.P.	7.5%
Glycol Salicylate	10%
Methyl Nicotinate	2%
Capsicin (Woolley)	0.1%
Base	ad 100%

POISON

Available in 1 oz. tubes 2/4 each * Basic N.H.S. price, also in Jars 4 oz., 8 oz., 16 oz. Basic N.H.S. prices 5/3, 10/3, 18/-.* * liable to purchase tax.

SALBIN (WOOLLEY)

JAMES WOOLLEY SONS & CO. LTD.
VICTORIA BRIDGE · MANCHESTER 3

in association with J. C. Arnfield & Sons Ltd.

WS1

A Superior Buffered Analgesic

'ALASIL' TABLETS—the improved form of salicylate medication—provide the efficient analgesia expected from their content of aspirin. Their superior acceptability derives from their content of a reliable buffer which minimizes the tendency to gastric irritation sometimes caused by the use of aspirin alone.

Advantages — 'Alasil' is an advanced sedative and antipyretic; it does not tend to induce gastric irritation; because of its high tolerability, it may be used for long-term administration even to those with sensitive stomachs, and to children.

Composition — 'Alasil' Tablets contain the recognized antacid corrective, 'Alocol' (Colloidal Aluminium Hydroxide), which permits their sedative principle, acetylsalicylic acid, to exert its action with minimal risk of side-effects.

Indications — Symptomatic pain, generally; rheumatism, fibrositis, lumbago, headache, dysmenorrhoea; dental pain.

Packs & Prices — TO PHARMACISTS (*P.T. exempt for dispensing*)
Standard size: 1000 in 250 bottles, 30/8.
'Juvenile' size: 375, 6/6; 750, 11/3; 1500, 21/6.

Alasil

NHS

M.391

Literature on request to:
A. WANDER LIMITED, 42 UPPER GROSVENOR ST., LONDON W.1

ALASIL JUVENILE TABLETS

Alasil 'Juvenile' Tablets specially sized for children, and neither coloured nor flavoured, are packed in tubes bearing dosage-for-age instructions.

ASTHMATIC, *YES...*

INVALID, *NO*

The balanced formula of 'Amesec' gives asthmatic patients a control which enables them to enjoy even the more vigorous forms of activity. By combination of one of the 'Pulvules' two or three times a day, with one of the 'Enseals' at night, 24-hour protection from attack is usually attained.

Each contains:—

Aminophylline	2 grs.
Ephedrine Hydrochloride	⅜ gr.
'Amytal' brand Amylobarbitone	⅜ gr.

'Amesec' is available as 'Pulvules' and as 'Enseals'

Lilly **'AMESEC'**

TRADE MARK

ELI LILLY AND COMPANY LIMITED, BASINGSTOKE, ENGLAND

Section of Pathology

President—Professor R. J. V. PULVERTAFT O.B.E., M.D., F.R.C.P.

Meeting
February 3, 1959

Cellular Associations in Normal and Abnormal Lymphocytes

(Illustrated by a Film)

PRESIDENT'S ADDRESS

By Professor R. J. V. PULVERTAFT, O.B.E., M.D., F.R.C.P.
London

COLLECTORS of Churchilliana may like to be reminded of the story of the pathologist who performed a blood count on him. On reviewing his troops, as the Prime Minister described the analysis of the differential count, he commended the polymorphs and monocytes for their meritorious service. "But what are these lymphocytes and eosinophils doing?" The pathologist admitted that he did not know—"but we find them very useful in the laboratory." "Sir", was the stern reply, "The human frame was built before the laboratory. Run away and find out what they are for." So far as I know, however, these orders have not yet been fulfilled, so difficult is it to extend a biological horizon.

It is indeed astonishing that no essential function has been ascribed to the lymphocyte. According to Osgood (1954) the human body contains 1,300 grams of lymphocytes outside the blood, lymph nodes, and bone-marrow; and Yoffey (1956) estimated that their weight in the bone marrow was 70 grams. Osgood again (1954) estimated that there were 3 grams in the circulating blood, and 100 grams in lymphatic tissue. The weight of the human liver is 1,600 grams, not very much more than the total weight of the lymphocytes. Yet Trowell (1958) could say at the end of his survey of the literature "it must be regretfully concluded that the office of this Cinderella cell is obscure".

I propose to discuss whether any suggestions derive from the study of the living lymphocyte collected from normal and pathological conditions. I shall do so in the main by presenting my material as a cinematographic record of some seven years' study, most of which has not previously been presented. This has been carried out as a combined operation with many colleagues, without whose help it would not have been possible.

At the very beginning I must emphasize that it is always a mistake to try to isolate the function of any cell in the body. Cells do not operate in a vacuum. We readily accept the interlaced pattern of hormones, reciprocally influencing endocrine organs; but all the organs of the body and all their cells are integrated. Perhaps indeed there is a simple mechanism whereby the chemical composition of all cells is kept basically uniform. In tissue culture cells may often be observed to sequestrate portions of their cytoplasm, and many, perhaps most cells, constantly take up from their environmental fluid small droplets by the mechanism known as "pinocytosis". In this way the special components of one cell may be, in however small a concentration, incorporated into the substance of others. In the case of many tissues "cell-lines" may be established and readily subcultured *in vitro*. We have isolated such strains from many types of pathological thyroids including carcinoma, from malignant melanoma, Hodgkin's disease, seminoma of testis, and fœtal human liver. We were late-comers in this field; but in common with all others we find that such easily cultivated cells quickly deviate from their early form to a primitive cell indistinguishable from the HeLa cell of Gey. Moreover in the case of the thyroid these cell lines cease to be able to synthesize hormones *in vitro*. They differ from the freshly isolated thyroid in many other ways; for example, in their reaction to certain viruses, in the rotation of the nucleus, and in the manner in which one cell is related to another (Pulvertaft *et al.*, 1959). It seems that at least in some cases normality can only be maintained when specialized cells are in constant relationship with others.

It is on the interrelationship of cells that I wish to focus attention. I shall consider the lymphocyte as a symbiont, if biologists will permit me to misuse a word not altogether appropriate in such a complex system as a living animal. From the enormous literature relating to this cell I shall extract at first two established facts only: first, that lymphcoytes are not uniformly distributed in the tissues, but characteristically are aggregated in foci; secondly, that they are motile. Motility in cells must imply a special function; we are in no doubt

what that function is in the case of spermatozoa, polymorphs and monocytes. When motility ceases, we must assume that the objective has been attained, as journeys end in lovers meeting. The cliché "round cell infiltration" establishes the fact that the wanderings of the lymphocyte are not invariably aimless, but that under certain conditions they clearly reach their destination and cease to move.

Parts of the film show that they move towards certain cells, and remain attached for long periods; if they leave they return again; their cytoplasm licks, as it were, the cytoplasm of other cells; in the cases shown these are malignant cells (Fig. 1). No other motile cell does this;

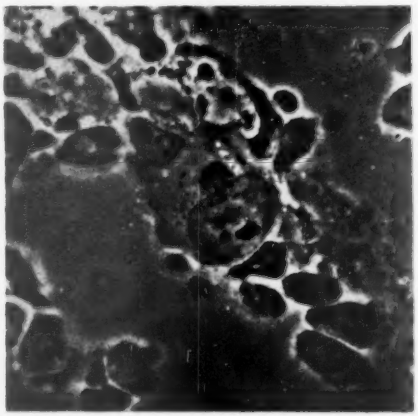


FIG. 1.—Lymph node, Hodgkin's disease. Serum agar. Adhesion of lymphocytes to Dorothy Reed cell. ×850.

Figs. 1–5 are all phase contrast photographs of living cells at 37° C.

for example the polymorph, the eosinophil and the monocyte never attach themselves to other cells in this way. It is true that we cannot deviate the lymphocyte from its apparently purposeless wandering by any chemical bait or by small particulate objects as we can so readily do in the case of the monocyte and polymorph. No one has ever established the existence of chemiotaxis in the case of the lymphocyte. When you see the lymphocyte moving in a time lapse or accelerated film you may be reminded of Graves' poem on the white butterfly:

> "The butterfly, the cabbage white,
> (His honest idiocy of flight)
> Will never now, it is too late
> Master the art of flying straight."

On the other hand, on occasions when the lymphocyte approaches close to certain other cells its movements are directed towards them. Dare we introduce a new word for this and call it "cytotropism"?

We first noted this kind of association in a "blunderbuss" examination of pathological material coming to the laboratory. Phase contrast microscopy opens our eyes to cellular detail which stained smears or sections exclude. We do not appreciate the fact that, with the exception of nucleated and adult red cells, practically every cell in the body is motile. We found that any motile cell tends to adhere to megakaryocytes, but that the lymphocyte differs in that once attached to megakaryocytes it never leaves them, whereas other wandering cells eventually escape. Obviously the megakaryocyte, like the platelet, is very sticky (Pulvertaft and Humble, 1956). It is, as it were, a cellular flypaper. The next feature we noted was that lymphocytes and only lymphocytes became attracted to areas of mitosis. Megaloblasts can be stimulated to divide by folic acid *in vitro* and when they enter into mitosis the lymphocytes are concentrated in their area. Most strikingly they tend to cross the dividing cells still united by a thread of cytoplasm; this gives a ludicrous appearance of "cutting the umbilical cord". Finally, whereas polymorphs, eosinophils and monocytes show no tendency to adhere to malignant cells, in many cases lymphocytes quite definitely do.

When freely suspended in fluid the lymphocyte adheres poorly to glass, indeed some people say that it does not adhere at all. It certainly does not spread out in the same way as a polymorph, and it is readily removed by washing the glass surface. It becomes elongated and detail in nucleus and in cytoplasm cannot be resolved. But when it is placed on a serum-agar surface (Pulvertaft *et al.*, 1956) and compressed under a cover-slip in a special chamber it behaves quite differently. In this case the depth of fluid is of the order of 50μ and it is repelled by the agar and attracted to the glass. It now becomes flattened out and moves characteristically, and its mitochondria can be clearly seen. However, it has been suggested that the adhesive phenomenon to which I have drawn attention may be an artifact, since large cells may produce a sulcus in the agar, and the lymphocyte may move around in the groove so produced. The greater part of the film was not taken with this type of chamber but in a different type in which agar is not used, but in which a small slide cell is made by sticking a ring made of plastic to a cover-slip and a slide. In these cells the lymphocytes move towards other cells and remain attached to them in exactly the same manner. We observed these associations as soon as we examined pleural exudates, malignant tissue, bone-marrow, and lymph nodes, for the

lymphocyte is ubiquitous, and most of our material came from cases of malignant disease. The most striking fact observed, however, was that occasionally the lymphocyte was found inside the cytoplasm of other cells, and that it circulated there for long periods. We gave the term "emperiopolesis" signifying "inside, round-about wandering" to this phenomenon (Humble *et al.*, 1956) (Fig. 2). When we first noted it we were unaware that we had long been anticipated. Indeed the process has been recorded cinematographically by Koller and Waymouth (1953). Trowell (1958) has collected many references.

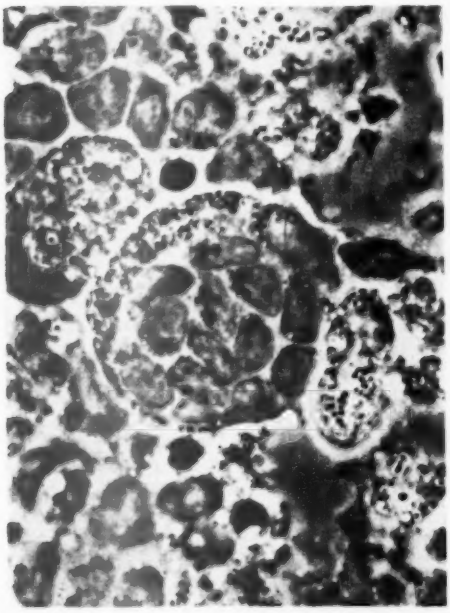


FIG. 2.—Intracellular lymphocytes in culture of human lymphatic leukæmic bone-marrow. Serum agar. ×885.

Some of these observations were made on stained preparations and these I think must be taken with caution, since it is hard enough to be certain of one's facts when living cells are examined. However, Fischer and Dolschansky (1929) observed the phenomenon in cultures of chick spleen. I take particular pleasure in recalling Dolschansky's work since, although my first introduction to tissue culture was in 1919 from Strangeways, it was Dolschansky who in Jerusalem taught me the discipline. Trowell (1949) saw it in mixed cultures of rat thymus and chick fibroblasts, and Darcy (1952) noted it on thyroid (homografts) in rabbits. These last two observations are of particular interest to me for my film deals with mouse thymus and chick fibroblasts as well as with human thyroids and lymphocytes taken from many sources. When we began our studies we were unaware of this earlier work; indeed, one of the interests of biological research is that all who undertake it find themselves irresistibly carried into the same channels, themselves often very bizarre.

Recently Emma Shelton and Mary Rice (1958) have isolated a strain of murine leukæmia in which the leukæmic cells are characteristically within histiocytes in the ascitic fluid which this form of murine leukæmia evokes.

So far as human cases are involved, the phenomenon is best seen both in the bone marrow and in the lymph nodes in cases of Hodgkin's disease and in lymphosarcoma. We have never seen it in normal bone-marrow or lymph nodes. We have examined many normal cases, the nodes being collected from gastrectomy cases suffering from peptic ulcer, and the bone marrow being selected from cases suffering from malignant disease not affecting the bone-marrow. It is customary to examine the bone-marrow before extensive radiotherapy is undertaken.

I therefore take it as established that the lymphocyte has been observed by many competent workers within other cells, and that in certain human diseases it can readily be so demonstrated in appropriate preparations when examined immediately after being set up. That is to say, it is not an artifact of culture.

I turn now to a different but closely allied matter, the duration of life of the lymphoctye *in vitro*. When explanted without other cells and in the conditions of these experiments that life is very short. I have been able to work through the courtesy of Dr. Hewitt with the strain of murine leukæmia isolated by him (1958). At 37° C. the life of these cells is measurable in hours or even in minutes. The cells very rarely indeed flatten themselves or move. A high proportion of them are in mitosis when first examined, but division never takes place. In twenty-four hours the cells have for practical purposes all autolysed.

Although there are a few examples of successful culture *in vitro* of murine leukæmia nearly everyone who has worked with the condition has failed. It would take far too long for me to relate all the variations of culture medium and technique which I have used in an attempt to prolong the life of these cells. I have even collected the cells and set up cultures in complete darkness. Embryo extracts, however concentrated, and whether from mouse or chick, do not extend the murine leukæmic cells' life. Horse, human or mouse serum, mouse ascitic fluid, yeast extracts,

lactalbumin hydrolysate, tryptic digests of serum, culture in pure oxygen, air, and pure nitrogen with the addition of 5% CO_2 all fail. Whenever I have read of a method recommended for culturing murine leukæmic cells I have used it, but always without success. Indeed, one of the very few, and certainly the first successful culture of murine leukæmic cells was that of De Bruyn (1949) where they grew only in the presence of mesenchymal cells; "a kind of symbiosis".

Lymphocytes collected from human reticuloses have *in vitro* and when by themselves as short a life as murine leukæmic cells, although human leukæmic cells are not so short-lived. If we pulp a lymph node in Hodgkin's disease or sometimes in lymphosarcoma the lymphocytes and other cells autolyse at 37° C. almost immediately. The process may be delayed by using soya bean trypsin inhibitor, but this is of limited value.

Lymphocytes from normal human lymph nodes and from many other sources, however, usually survive much longer. As a rule they are fully motile for twenty-four hours, and often survive for four days by themselves. There is continuous autolysis, and at the end of a week the survivors become very large, non-motile, and quite unrecognizable. There is much controversy as to the final destination and morphology of this cell and I shall not further discuss this question here. The significant fact is that the vast majority autolyse within four days. The vulnerability of the lymphocyte is exemplified by its reaction to radiation, since relative lymphopenia is an early indication of radiation damage. This can be demonstrated *in vitro* (Humble *et al.*, 1954). Since I shall develop the argument that lymphocytes and malignancy are closely associated, it is tempting to suggest that some of the beneficial results of radiotherapy may be associated with destruction of lymphocytes.

The picture is very different when other tissues are present. One experiment which I carried out particularly impressed me. I took a very early whole mouse embryo about 2 mm. long and incorporated it in chick fibrin with a portion of murine leukæmic thymus. In a day or two these fragments fused, and the embryo heart continued to beat for six weeks. There was a moderate outgrowth of fibroblasts, but the cells of this chimæra for the most part did not migrate into the fibrin clot. The leukæmic cells could be clearly identified in large numbers and over the course of weeks infiltrated into the embryo tissue and could be recognized around the heart. It appeared that the leukæmic cells slowly increased in number. I cannot tell how long they would have survived had I contented myself with replacing the fluid medium. Unfortunately at the end of six weeks I added fresh chick plasma in order, as I thought, to help the leukæmic cells to migrate. This they did, as well as fibroblasts from the chick embryo. The heart ceased to beat and the migrating leukæmic cells quickly lysed when they had wandered away from the embryo and into the fibrin clot.

In this case, therefore, I had observed a strikingly long survival of the leukæmic cells when other tissue was present. I had noticed the same phenomenon many times in human tissues *in vitro*. For example, malignant melanoma is very readily cultured *in vitro*, and the tissue explanted often contains lymphocytes. I have noted survival of human lymphocytes for six weeks under these circumstances. Human thyroid gland is also quite exceptionally easy to maintain alive *in vitro* (Pulvertaft *et al.*, 1959) and often contains lymphocytes. These are found alive after many weeks.

These observations stimulated an attempt to discover how murine and human lymphocytes would behave when presented with monolayers of other cells. The preparation of monolayers is to-day a routine technique among virologists. They are easily prepared by trypsin dispersal (Dulbecco and Vogt, 1954). Not all tissues are equally suitable but mouse and chick embryo or chick fibroblasts are very suitable and, fortunately, human thyroid. I say fortunately because human thyroid tissue is readily available from the operating theatre. Moreover, it survives for many weeks and does not multiply *in vitro* until what is known as transformation takes place. Embryo tissue unfortunately multiplies *in vitro* within a few days of setting up experiments, and this overcrowding of culture chambers sets a limit to the duration of experiments.

The results were quite convincing. When the

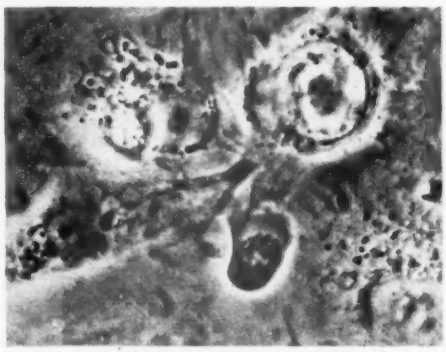


FIG. 3.—Human chronic lymphatic leukæmic cell from blood, with human thyroid. Lymphocyte between thyroid cells and cover-slip. Ring culture in fluid. ×850.

lymphocytes at first sedimented on to the cell sheets they were evenly distributed, but within a few hours as a rule aggregated into clumps. The individual cells remained spherical, but moved around each other. At the end of eighteen hours the picture was quite different.

I may take as an example two cases of cells from human lymphosarcoma which came for examination within a short time of each other. The cell sheets on this occasion were chick embryo. The lymphosarcomatous cells were in eighteen hours concentrated entirely around the areas where there were embryo cells. The sheet was discontinuous, and where there were no embryo cells, there were no lymphosarcoma cells. Most of the lymphosarcoma cells were clearly within the embryo cells. Later these experiments were repeated using human thyroid sheets and cells from a buffy coat from chronic lymphatic leukæmic blood and from the bone-marrow in late lymphosarcoma. In this case the lymphocytes moved freely between the cover-slips and the cell sheets, that is to say the lymphocytes were originally in the free fluid above the thyroid cells, and in eighteen hours were all between them and the cover-slips (Fig. 3).

A large number of tests were then carried out using murine leukæmic cells of Hewitt's strain. As a rule the lymphocytes were obtained from the thymus and in the original experiments sheets of chick or mouse embryonic cells were used as a source. The leukæmic cells were clearly seen to have penetrated the embryo cells, and they divided within those cells on many occasions. Individual leukæmic cells were also seen to autolyse within the embryo cells (Figs. 4 and 5). Survival of the leukæmic cells was noted for many weeks, although the experiments were invariably terminated by crowding of the culture chambers through cellular multiplication, and on no occasion was subculture successful.

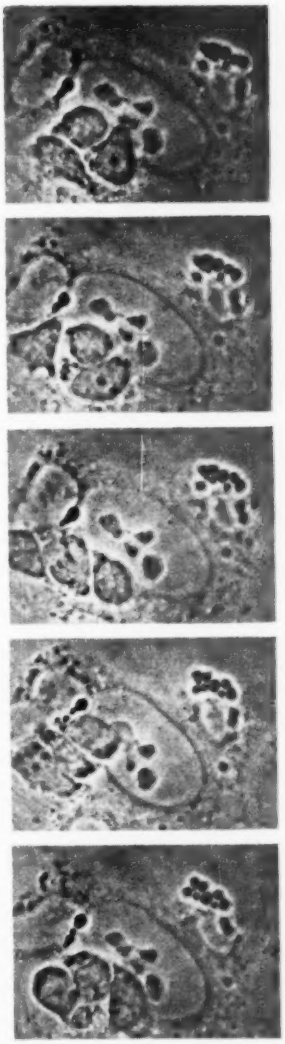


FIG. 4.—Murine leukæmic cells with chick embryo. Penetration of embryo cells. Ring culture in fluid. ×780.

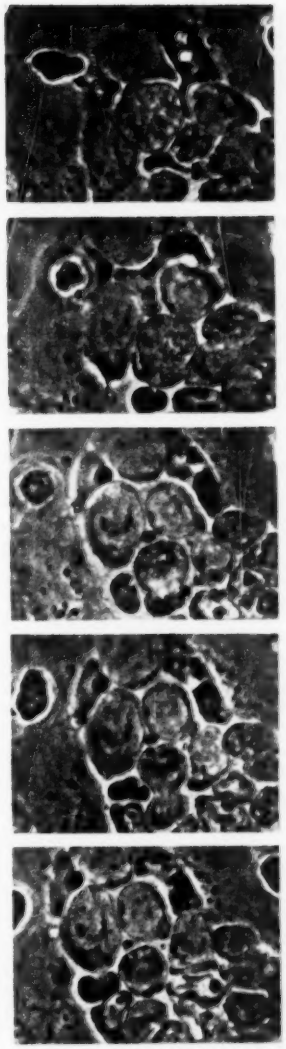


FIG. 5.—Murine leukæmic cells with chick embryo. Multiplication and lysis within embryo cells. Ring culture in fluid. ×780.

Similar results were found with human thyroid sheets, although penetration of thyroid cells was not observed. The movement was apparently always between cover-slips and thyroid cells, but the long survival was equally clear. The experiments here were terminated by the death of the thyroid cells in about a month.

I should make it clear that only a very small proportion of the murine leukæmic cells actually survived. Several can sometimes be seen in one field but the majority autolyse and only those which establish themselves under the thyroid cells survive.

This may be a suitable place to define the criteria for judging that lymphocytes are truly intracellular. I do not think that it is possible to be certain about this in stained preparations. In living preparations unequivocal evidence is provided only when the lymphocytes are seen to move over a nucleus and under a cytoplasmic granule of the investing cell, and where the limits of the investing cell are never transgressed. This I have frequently seen; the granule, the lymphocyte and the nucleus of the investing cell are in three superimposed optical planes and for this reason the appearance is less decisive in cinematographic record than it is to the observer of the tissue culture. Less conclusive, but to my mind quite satisfactory evidence, which is often seen in my film, is available when lymphocytes circulate always within the perimeter of one investing cell, displacing its cytoplasmic granules and distorting its perimeter.

The more frequently observed phenomenon is the penetration of leukæmic cells and lymphocytes through cell sheets and between those sheets and the glass cover-slip. It is difficult to understand in what medium they are now moving as the cell sheets are quite firmly adherent to the glass, and often require trypsinization for complete removal; in many cases they cannot be washed off with culture medium alone. The leukæmic cells and lymphocytes can be seen to squeeze between cells in a remarkable and almost indescribable manner. When cell sheets are touched with a glass rod they often retract, but the presence of the lymphocytes never disturbs them.

Hamster mesentery flattened over agar also makes a good cell sheet and the lymphocyte moves between the cover slip and the mesentery in exactly the same way.

When fully extended on glass lymphocytes and leukæmic cells are quite unrecognizable to an observer familiar only with stained preparations. They cover surprisingly large areas, and the nuclei are markedly patterned. The leading edge of the cytoplasm characteristically bulges, now in one direction and now in another, and the prenuclear cytoplasm is always free of organoids. These trail behind, usually in a pointed tail. Lymphocytes appear to attract each other when inside cytoplasm and under cell sheets where, even when present in small numbers, they constantly converge towards each other. Since by nature of the experiment the field is always illuminated, phototaxis is not ruled out, or even a small local rise of temperature in spite of a heat filter which is always used.

The lymphocytes in Hodgkin's disease and acute leukæmia may show very large granules which by phase contrast are very dark; these do not stain in Leishman films. Transitional forms of lymphocytes and plasma cells are often seen. The plasma cells in myelomatosis move sluggishly and they are unique in my experience because the nucleus is trailed behind. Again in lymphosarcoma, although these cells in general resemble lymphocytes, on occasions an undulating "organdie" edge of cytoplasm may be seen which resembles the movement of monocytes.

I do not wish to confuse my narrative by undue reference to other experiments but it is perhaps permissible to add that certain mouse ascites tumours such as S37 behave in my hands like the leukæmic cells in that they cannot be cultured alone but survive well on cell sheets, and that I have an indication that certain human malignant material, such as carcinoma of the breast, may behave in the same way.

The results show that the lymphocyte is attracted to other cells and cannot long survive without them, may enter into their cytoplasm, may there divide and may there autolyse. And I ask, how does this behaviour fit in with or throw light on familiar facts in the natural history of leukæmia and malignant disease?

I begin with the familiar association between malignant metastases and lymphoid tissue. This of course is often held to be an attempt by the reticulo-endothelial system to remove foreign cells; as we all know it is an unsuccessful attempt. In my hands when malignant cells are collected from metastases in lymph nodes they survive very well, while a primary growth in the breast survives very poorly. Malignant cells in serous exudates where lymphocytes are always present survive reasonably well.

Again we often find in sections a close association between malignant disease and round cell infiltration. One type of carcinoma, the lymphoepithelioma of Régaud, is characteristically rich in lymphocytes. I have seen two cases of chronic lymphatic leukæmia in squamous cell carcinoma on top of leukæmic deposits in skin (Pulvertaft, 1936).

However, undoubtedly the work of Gross and his successors on mouse leukæmia is in this context the most stimulating. Gross (1951) found that malignant tumours could be induced in the progeny of mice inoculated with centrifugates of leukæmic tissue. In his hands leukæmia as well as malignant disease was conclusively produced with these cell-free filtrates. This work has had much confirmation and I would like to refer in particular to the very recent work of Salaman (1959) who finds that newborn mice inoculated with centrifugates of leukæmic blood themselves after short latent periods develop more than one

type of malignant disease, but not leukæmia. There is a large body of confirmatory evidence on this most significant discovery and, although several workers have failed, it seems clear that this failure is more likely to be due to variation in technical method and in strains of mice than to any other cause. It is clear as Salaman emphasizes in his review that, where donor and recipient mice differ antigenically, induced leukæmias and tumours have been of recipient cell type and not of donor.

In Salaman's own series 40 tumours appeared in 15 out of 23 inoculated mice which survived three weeks or more—the first tumour after eleven weeks. The tumours included carcinoma apparently of salivary glands and of mammary tissue in males as well as females. Metastases were found in the lungs. There were also four sarcomas. It is even suggested by certain workers, such as Hays *et al.* (1957) and Latarget *et al.* (1958) that extracted nucleic acid alone may be effective. There are further suggestions that the lymphocytes may enter other cells and be re-utilized for the manufacture of new lymphocytes in the work of Hamilton (1954, 1956): his experiments indicate that some lymphocytes survived eighty-five days, and that others either had a half-life of three hundred days or were used by stem cells for the production of fresh lymphocytes.

To sum up, normal lymphocytes when alone have a short life; supported by other cells, a long one. "Malignant" lymphocytes have frequently a still shorter life in tissue culture; but here again when in symbiosis their life term is greatly extended. There is a close analogy also between their behaviour and the life of certain parasites such as protozoa and viruses.

Lymphocytes, whether normal or malignant, apply themselves closely to other cells, and are in some cases attracted by malignant cells; the cytoplasm of lymphocytes appears at time to be "licking" that of the malignant cell.

"Malignant" lymphocytes are often found inside histiocytes when first collected from cases of reticulosis. They move inside them, not in vacuoles, but freely in the cytoplasm. "Malignant" lymphocytes readily invade tissue cultures of chick and mouse fibroblasts, and are found freely motile inside their cytoplasm in considerable numbers. In murine leukæmia they divide and autolyse within embryonic cells.

There is a distinction between the behaviour of lymphocytes with thyroid sheets and embryonic sheets. I have never observed penetration of thyroid cells, but only movement between them and the cover-slip, while in the embryonic cells there is obvious cellular penetration.

A large series of lymph nodes and bone-marrow preparations has been examined in which there was no diagnosis of malignant reticulosis; in no case was there evidence of histiocytes with included lymphocytes when freshly examined. On the other hand, all lymphocytes, normal and abnormal, penetrate between sheets of cells and cover-slip.

It may be suggested that there is some special property of embryonic cells and of thyroid cells by virtue of hormone production, which encourages longevity of lymphocytes. I have no observations which might support or contradict such a suggestion.

A profoundly significant fact is that neither I nor any other observer has recorded any cell except the lymphocyte as living and moving within histiocytes. Polymorphs, eosinophils, monocytes and many "blast" cells were present in a number of my preparations, but only lymphocytes were found intracellularly. The moment of penetration was never seen; but from examination of film sequences I am convinced that histiocytes on occasion become enormously extended in thread-like form; the long process becomes curved around a group of lymphocytes, and later the ends of the cytoplasmic thread become joined up; eventually the vacuole thus formed becomes filled in by the cytoplasm of the histiocyte. I believe that the histiocyte is in part at least the aggressor.

We must ask ourselves in what way these observations may be related to the development and propagation of the malignant process. Here we enter the realm of hypothesis, and I do so without apology, for observations and experiments are useless unless they point the way to new conceptions. Research is like "blind man's buff": we touch our target for a moment in the darkness but can neither hold nor name it; only at long last do we grasp it firmly and claim with confidence to recognize it without a doubt. For most of the time we must be content with half-knowledge and uncertain guesses. At any one time "the truth" is merely the closest approximation to reality which we can attain in the light of our present knowledge.

One of the functions of the lymphocyte may be to bring to selected areas concentrations of enzymes and of nucleic acid. The lymphocyte has a cycle; it is derived from stem-cells in lymph nodes and in the reticulo-endothelial system generally, and returns to that system for re-utilization of its specialized chemical components.

The lymphocyte may, like every other cell, become malignant; it is no part of our argument to say how or why. Once malignant its nucleic acid is carcinogenic, and by incorporation into another cell imposes malignancy on that cell.

In the case of lymphatic leukæmia or lymphosarcoma penetration of a stem cell induces the

production of malignant descendants. But we may envisage a state of affairs in which a stem cell may be "invaded" at a stage in which some degree of differentiation had already taken place. In such a case, the adult cells derived from this "invaded" cell will be of various types and we find, as in Hodgkin's disease, a pleomorphic malignant picture with "malignant" polymorphs, eosinophils, monocytes and lymphocytes.

In murine leukæmia the extracts of the malignant lymphocytes display the widespread carcinogenic potency of the "malignant" nucleic acid; not only malignant lymphocytes, but also mammary, salivary gland and connective tissue malignancy are induced. Successful experiments have so far only been performed on newborn mice; and carcinogenic power of lymphocytes in adult animals is not suggested, so far as I know, by any recorded work.

If, however, we examine human malignant tissue in paraffin sections determined to incriminate this cell we can find it guilty at least of association. Anyone who cares to can examine the point at which a Grade I carcinoma of rectum invades normal epithelium and here he will always find large accumulations of lymphocytes. At this point too, he will never find a transition between the mucin-forming normal columnar epithelial cell, with a small basal nucleus, and the malignant cell, with its cytoplasm practically full of nucleus. What is happening? Is the normal tissue just pushed aside by the extending and multiplying malignant tissue? Or is there any possibility that "normal" cells, at this point, are being transformed into malignant cells? If so, by what mechanism? Could it be by invasion by lymphocytes?

Trowell (1958) has collected many references to the existence of lymphocytes within epithelial cells, e.g. Kelsall (1946), Andrew and Burns (1947), Andrew and Andrew (1949). I have no difficulty whatever in identifying lymphocytes apparently within normal epithelial cells at the junctional point of normal and malignant rectal epithelium.

It is regrettably only too easy to support any hypothesis, however preposterous, with selected evidence. A thousand observations contradict the notion of continuous transformation of cells by a continuously acting agent of any kind. Only perhaps in a Presidential Address, where convention frowns upon discussion and contradiction, could such a suggestion be made: and then only with the admission that it is taking an unfair advantage of a long-suffering audience. All I can really claim, with confidence, to have shown is the dependence of all lymphocytes on other cells for survival, and their power of survival inside other cells when "malignant". What light this fact throws on the nature of malignant disease must be for others to determine. It may be that the lymphocyte holds within it the keys of life and of death.

Acknowledgments.—I have to thank many collaborators for their help. Dr. H. B. Hewitt and Dr. J. G. Humble have continuously supplied me with material and collaborated in many of the experiments. Dr. J. T. Groves, Dr. J. Davies, Mr. Howard Jayne, Dr. L. Weiss, Dr. W. H. Wilkinson and Dr. C. H. Wilson have collaborated in many of the experiments. Dr. D. H. Mackenzie has supervised the collection in a fresh state of the surgical material. Dr. Peter Hansell and Mr. R. McV. Weston have guided me in cinemicrography. I have made the fullest use of the critical reviews by Dr. O. A. Trowell and Dr. L. H. Salaman.

Mr. J. A. Haynes has throughout afforded technical assistance and advice and undertaken the heavy duty of editing and cutting the film.

The expenses were covered in the main by the British Empire Cancer Campaign, and in part by the Governors' Discretionary Fund of Westminster Hospital.

REFERENCES

ANDREW, W., and ANDREW, N. V. (1949) *Anat. Rec.*, **104,** 217.
——, and BURNS, M. R. (1947) *J. Morph.*, **81,** 317.
DARCY, D. A. (1952) *Phil. Trans.*, B, **236,** 463.
DE BRUYN, W. M. (1949) *Bijdr. Dierk.*, **28,** 77.
DULBECCO, R., and VOGT, M. (1954) *J. exp. Med.*, **99,** 167.
FISCHER, A., and DOLSCHANSKY, E. (1929) *Arch. EntwMech. Org.*, **116,** 123.
GRAVES, R. (1936) Flying Crooked. Faber Book of Modern Verse. London.
GROSS, L. (1951) *Proc. Soc. exp. Biol., N.Y.*, **76,** 27; **78,** 342.
HAMILTON, L. D. (1954) *J. clin. Invest.*, **33,** 939.
—— (1956) *Nature, Lond.*, **178,** 597.
HAYS, E. F., SIMMONS, N. S., and BECK, W. S. (1957) *Nature, Lond.*, **180,** 1419.
HEWITT, H. B. (1958) *Brit. J. Cancer.*, **12,** 378.
HUMBLE, J. G., JAYNE, W. H. W., and PULVERTAFT, R. J. V. (1956) *Brit. J. Hæmatol.*, **2,** 283.
——, ——, —— and WILSON, C. W. (1954) *J. Fac. Radiol.*, **5,** 16.
KELSALL, M. H. (1946) *Anat. Rec.*, **96,** 391.
KOLLER, P. C., and WAYMOUTH, C. (1953) *J. R. micr. Soc.*, **72,** 173.
LATARGET, R., REBEYROTTE, N., and MOUSTACCHI, E. (1958) *C.R. Acad. Sci., Paris*, **246,** 853.
OSGOOD, E. E. (1954) *Blood*, **9,** 1141.
PULVERTAFT, R. J. V. (1936) *Brit. J. Surg.*, **24,** 50.
——, DAVIES, J. R., WEISS, L., and WILKINSON, J. H. (1959) *J. Path. Bact.*, **77,** 19.
——, HAYNES, J. A., and GROVES, J. T. (1956) *Exp. Cell Res.*, **11,** 99.
——, and HUMBLE, J. G. (1956) *Rev. Hémat.*, **11,** 349.
SALAMAN, M. H. (1959) *Brit. J. Cancer* (In the press).
SHELTON, E., and RICE, M. (1958) *J. nat. Cancer Inst.*, **21,** 137.
TROWELL, O. A. (1949) *J. Physiol.*, **110,** 5P.
—— (1958) *Int. Rev. Cytol.*, **7,** 235.
YOFFEY, J. M. (1956) *J. Histochem. Cytochem.*, **4,** 516.

SEDATION WITHOUT DRUGGINESS

PARABAL

Reduces phenobarbitone intake to one sixth without loss of sedation.

50 tablets cost 2/3d. basic N.H.S.

Each tablet contains 260 mg. Phenobarbitone Sodium Dihydroxyaluminiumaminoacetate.

Samples and literature on request.

WEST PHARMACEUTICAL COMPANY LTD

9 Palmeira Mansions Church Road Hove 2 Sussex

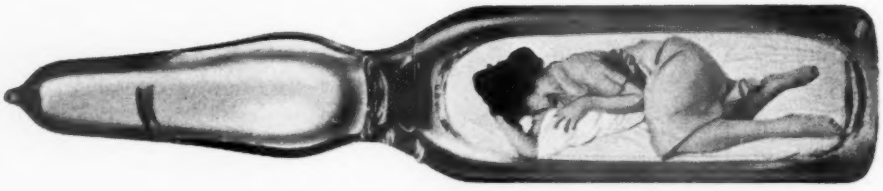
Telephone Hove 70606

when immediate control is imperative

in nausea and vomiting . . .
and in acute psychotic episodes . . .

Fentazin Injection

PERPHENAZINE



rapid response
fewer hypotensive effects
freedom from pain
virtual freedom from side-effects

Fentazin is an unusually effective psycho-therapeutic and anti-emetic agent. When intensive and rapid treatment is needed, Fentazin may be given parenterally. Fentazin Injection has important clinical advantages.

It is normally effective within ten minutes of injection: maximum effect is produced within one or two hours. Significant hypotension is very rare—an important advantage in pregnant women, elderly patients, and surgical cases. Fentazin Injection can be administered slowly by deep intramuscular injection, without causing pain or distressing local reactions.

As with oral Fentazin, side-effects are minimal.

Fentazin Injection contains 5 mg. perphenazine in each one cc. Ampoules of 1 cc. in boxes of 5 and 100 (5 x 20).

A H

ALLEN & HANBURYS LTD LONDON E2

'Fentazin' is a Trade Mark
AH50

Section of Anæsthetics

President—H. J. V. MORTON, M.D.

Meeting
December 5, 1958

An Evaluation of General Anæsthetic Techniques for Use in the Dental Surgery

By W. S. MCCONNELL, M.B., F.F.A. R.C.S.
London

IT cannot be denied that the quality of chair-side anæsthesia often falls short of that which is achieved in an operating theatre. A dental surgeon may start his work with doubts about finishing it under adverse operating conditions, and the anæsthetist sometimes gives him the impression that he must "do his best" however unsatisfactory the circumstances. Some anæsthetists dislike "giving a gas". They are happy and phlegmatic while a surgeon has a finger in the heart or draws the cut ends of an œsophagus together, but are ill at ease and uncomfortable when confronted with a patient in the dental chair. The reason for this change of outlook is surely that all available aids to good anæsthesia are at finger-tip control except at the chairside.

In the operating theatre all he need do is to inject more of a selected drug into an open vein or alter the contents of the mixture inspired by or squeezed into the patient. Furthermore, he has available all the details of the patient's medical history and the results of any investigations. Thus in an operating theatre an anæsthetist has the power of any chosen drug, and the knowledge of the human material on which he is working, but at the chair-side he may feel impotent and ignorant.

The Discontent of Dental Surgeons and Anæsthetists

The major criticism of the dental surgeon is that the operating conditions range from poor to impossible. Failure to complete the extractions is usually projected on to the dental surgeon, when in fact he had but little chance of success with a moving target. It is inexcusable for the anæsthetist to remain silent in these circumstances and allow the dental surgeon to take all the blame. I have prevented a dental surgeon from putting a finger in the mouth of a patient fighting madly under nitrous oxide: the honest explanation that the anæsthetic I had chosen was quite unsuitable was accepted, and the dental surgeon was thanked for not attempting the extraction.

Anæsthetists must strive to abolish the criticism of a chairside assistant whose comment was: "I would never have gas. I was a dental nurse at a hospital in London, and having worked in the gas rooms, it has put me off for life."

If better operating conditions are not provided by general practitioners or anæsthetists, the dental surgeons will give their own anæsthetics. There are already several societies whose aim is to train dental men in anæsthetic techniques at the chairside.

Anæsthetists criticize dental surgeons for planning work under general anæsthesia without regard for the risks involved. An important part of the duty of the anæsthetist is to act as a filter of fitness and an assessor of adequate preparation before anæsthesia. I have been confronted with a patient whose first outing after bed rest for coronary thrombosis was to the dental chair. I antagonize dental surgeons by refusing to give an anæsthetic to a patient who has had a recent meal, for I am unwilling to sacrifice safety to convenience. In exchange for the help in assessing the patient's condition, the dental surgeon should concede to the anæsthetist a veto on unwise or untimely anæsthetics in the chair.

The Demand for Time and Tranquillity

Continuous nasal nitrous oxide and oxygen has been in use from the beginning of the century, but a turning point was marked thirty years ago when John Winter, an American dental surgeon, came to this country to demonstrate the removal of impacted lower third molar teeth with hand chisels and levers. Winter, by careful selection of cases, sharp instruments and great skill required only five to ten minutes' anæsthesia,

but his imitators demanded what came to be known as "the long gas". At dental hospitals with no provision for in-patients, difficult lower impacted 3rd molars were attempted under unassisted nasal nitrous oxide-oxygen anæsthesia, and the skill of the anæsthetist was measured by the length of time he could keep the patient quiet and still. To my shame I admit keeping an easy patient in this condition for 90 minutes. I need not dwell on the folly and danger associated with this attempt to obtain time and tranquillity: the condition of the patients afterwards made certain they would only submit to it once. A distinguished colleague gave a superb "long gas" in the chair to the queen of a European country. Her feelings afterwards were shown by the reward of cuff-links and not the usual signed photograph.

With the introduction of the first short-acting intravenous barbiturate, hexobarbitone sodium (Evipan), in 1932 the scope of dental anæsthesia was widened, but the question whether this potentially lethal injection should be given to ambulatory patients sitting upright in the dental chair produced widely differing opinions. The correspondence columns of the *Lancet* (1934) treated the subject as "The Battle of the Barbiturates". After a quarter of a century the situation obtains where some would say not to give an intravenous barbiturate to a patient in the dental chair is old-fashioned, but others regard it as near-criminal folly.

My plea is that our minds should not be shut to the introduction of any new drug or technique which an enthusiast is attempting to use for anæsthesia in the dental chair. We should be thankful to those who introduced into dental anæsthesia the intravenous barbiturates, divinyl ether, premedication for the ambulatory patients, cyclopropane, trichlorethylene, intravenous pethidine, the ultra-short-acting barbiturates (buthalitone), and Fluothane.

It is doubtful whether an ideal universal dental anæsthetic will be evolved for two reasons: the variations in age, nature and whims of the patient, and secondly the extent and difficulty of the dental work in relation to the skill of the operator. The age range of my patients is from 96 weeks to 96 years, their nature from frail little women to overweight alcoholics, and their whims from refusal of inhalation methods to an absolute objection to the prick of a needle. Not only must the anæsthetic be "tailored" to the patient, but also to the skill of the operator. I have knowledge of the ability of 140 dental surgeons, some of whom can extract four 6-year-old molars for a 12-year-old boy under unassisted nitrous oxide-oxygen anæsthesia, and others who cannot.

The Use of Pre-anæsthetic Sedatives

Children.—In my experience 90% of children are co-operative and therefore the routine sedation of all young patients is not justified. When a child between the ages of 5 and 12 years will not respond to an emotional or logical appeal for co-operation, a pre-anæsthetic sedative may turn the scale from failure to success. Such sedation has abolished dragging a howling child to the dental chair. On many occasions I have provided a sedative for a child who will not sit in the dental chair and returned in one hour to find a dizzy but tractable patient.

The careful investigation by Goulding *et al.* (1957) into the behaviour of children a few moments before anæsthesia is induced in the dental chair stresses the importance of using an adequate dose of a sedative if it is to be effective. Goulding found that small doses of a barbiturate, methylpentynol or chlorpromazine did not alter the behaviour pattern of small children when compared with an inert substance: if, however, a sufficient dose of any one of these drugs is given, an amenable patient will certainly result. Many drugs are suitable as pre-anæsthetic sedatives, and good results have been claimed from opium (as Nepenthe), the tranquillizers and the recently introduced trimeprazine elixir (Vallergan). One of the easiest to use is quinalbarbitone (Seconal), now conveniently prepared as a sugar-coated tablet.

The advantages of pre-anæsthetic sedation are the ability to turn an unco-operative child into one who will submit to inhalation anæsthesia, and in addition the sedation permits a higher proportion of oxygen to be given during nitrous oxide anæsthesia. The drawbacks to sedation are the additional time and trouble required in administration and the occasional unpleasant after-effects. Time is required for a specific visit to see the child at a dental surgery and assess the dose of sedative drug. In my experience it is unwise to guess at a dose and send it to a parent with instructions when it should be given, for untoward effects may follow during the journey to the dental surgeon. Occasionally undesirable effects are seen after anæsthesia in the sedated child. It may cry without reason, fail to obey commands and cannot be comforted by a sensible mother. This period may not be remembered by the child, but the disturbance does magnify what should be a small incident into a major event.

Adults.—It is a matter of opinion whether sedation of a nervous adult to tolerate inhalation anæsthesia is justified by the uncertain results.

Provided there is no contra-indication, I favour using an intravenous agent in the borderline apprehensive adult. I have used heavy sedation by mouth in cases which present special difficulties, for example, patients with bronchiectasis or severe bronchitis. It is possible to give a patient whose gaseous exchange is poor a satisfactory nitrous oxide-oxygen mixture after effective barbiturate sedation.

Inhalation Anæsthesia for Infants and Small Children

The duration of anæsthesia required for the extraction of teeth in babies and children up to 4 years of age is brief, and it is thought unwise and unnecessary to use sedation with resultant drowsiness for some hours in conjunction with an anæsthetic which may be given for some seconds only.

Three anæsthetic agents are in common use for babies and small children: (1) Ethyl chloride given on an open mask, (2) Nitrous oxide and oxygen from a standard machine, (3) Divinyl ether (Vinesthene) from a closed inhaler.

Ethyl chloride has three serious disadvantages. The first is the risk to life from circulatory depression for the margin between anæsthesia and arrest of respiration and circulation is small. The second drawback is the frequency of the onset of a troublesome laryngeal spasm however skilfully the drug is administered. The third objection is the high incidence of nausea and vomiting which may follow even brief periods of ethyl chloride anæsthesia. In my opinion the intrinsic disadvantages of the drug outweigh the advantages of convenience. My only use for ethyl chloride is to tide over an unexpected difficulty such as sudden loss of co-operation and mouth breathing in an older child during induction with nitrous oxide.

Nitrous oxide and oxygen is difficult and dangerous to administer to babies and small children. Because the minute respiratory volume is high and the circulation time is short, the hazards of anoxia can occur suddenly. As it is unusual for a small child to tolerate a dental prop before induction of anæsthesia, oxygen lack may result in the parlous state of masseteric spasm, opisthotonus and profound cyanosis.

Divinyl ether is commonly used in a closed bag such as the Oxford modification of the Goldman inhaler. Gray and Halton (1951) criticize such closed inhalers for two reasons. The first is the psychological trauma which may be produced when the stifling sensation of a full face mask, augmented by the pungent smell of Vinesthene, confronts the child. The second objection is the probability that re-breathing into a closed bag will cause carboxæmia and anoxia. I am an unrepentant user of Vinesthene in an Oxford inhaler, and it has been my anæsthetic of choice for infants for the past twenty-three years. Provided the child is not forced to rest the head in a particular position (whether seated on cushions in a dental chair or nursed in the crook of the left elbow of a chairside assistant) it is possible to present the face mask below the chin, tire out the sense of smell and eventually obtain a gas-tight fit without a conflict.

The freedom from anxiety during anæsthesia and the almost unbelievable absence of after-effects are the merits of divinyl ether. I blame myself and not the drug if a small child is not prepared to take my hand and walk from the dental chair after anæsthesia.

Should the number or difficulty of the extractions demand a longer period of anæsthesia than can be obtained with a "one shot" method, nasal nitrous oxide and oxygen can be given from the moment the Vinesthene inhaler is removed. The divinyl ether absorbed during induction allows sufficient oxygen to be given with nitrous oxide to flatter the anæsthetist, whose patient is both pink and tranquil. Dawkins (1958) has recently called attention to the remarkable record of Vinesthene as a safe anæsthetic: his figures show a mortality of less than one in half a million cases.

Larger Children

The average-sized child of 5 years of age may be given nasal nitrous oxide and oxygen supplemented by Vinesthene. An ampoule of the drug may be emptied into the reservoir bag, or 5 ml. from a syringe may be injected through a Mitchell needle previously inserted into the nose-piece tubing of the apparatus. By allowing the child to lose consciousness with nitrous oxide before the Vinesthene is given, the objection to the unpleasant smell is avoided.

For children in their teens unassisted nitrous oxide and oxygen is satisfactory. I am continually amazed at how little disturbance is produced by such "controlled anoxia". When using nitrous oxide for the larger child it is reasonably certain that no pain of the extractions will be felt, but the initial good position of the head may be lost if a wriggle or a reflex movement occurs. A chin-on-the-chest attitude may be obviated by the use of a "lap strap". In my experience the adjustment of a retaining belt over the upper ends of the thighs causes little disturbance to the patient

as it is routine practice in aircraft and may well become so in motor cars. If a strap over the thighs and under the seat of the chair is tightened after consciousness is lost, it will keep the pelvis of the patient firmly against the back of the chair and prevent forward slide which upsets the position of the head. I have no hesitation in using a lap strap if the dental programme—for example, the removal of four 6-year-old molar teeth—is likely to be difficult.

The Dangers of Oxygen Lack with Nitrous Oxide

Is an experienced anæsthetist likely to see the results of oxygen lack in the routine use of unassisted nitrous oxide-oxygen anæsthesia? In my experience the answer is "Yes" for perhaps in 1 of 2,000 cases the patient will unexpectedly become cyanosed, an engorged tongue obstructs the airway and respiration stops. The colour of the patient becomes blue-grey, the tongue feels like cold uncooked meat and the radial pulse is difficult to detect. This anoxic state is a grave threat to the life of the patient, but I still find difficulty in getting the dental surgeon's fingers (plus a throat pack) out of the mouth in the early stages of its onset. An adult patient usually recovers from this hazard within five to ten minutes, but I can recall cases in which the feelings of air-hunger, nausea and faintness took longer to subside. In children, nitrous oxide and insufficient oxygen—as shown by continued cyanosis—may result on recovery in disorientation, screaming for no apparent reason, refusal to obey commands and failure to respond to a comforting mother.

Two techniques have been suggested to avoid oxygen lack with nitrous oxide anæsthesia:

(1) "*Amnalgesia.*"—Tom (1956) describes this as a state between analgesia and delirium during which extractions may be performed without pain or without the memory of pain. The patient inhales a few breaths of pure nitrous oxide then 18 to 20% oxygen is added. After about 40 breaths of this high oxygen mixture the eyelids are relaxed, the expression of consciousness in the eyes is lost and the patient breathes quietly, free from stertor, jactitation and cyanosis. It is claimed that even if the patient responds to stimulation by movements, there is no memory of pain.

(2) Mostert (1958) advises washing out the nitrogen from the lungs with oxygen. To achieve this result, high flow rates of pure oxygen are necessary if re-breathing is to be avoided, and the process may take two minutes. Nitrous oxide is then given in the proportion of 80–85%, and the patient will remain under tranquil anæsthesia without cyanosis for several minutes. A careful explanation of the technique must be given before induction if he is not to be disconcerted by the seemingly long wait for the onset of anæsthesia.

A possible explanation of an unexpected collapse of a patient during nitrous oxide anæsthesia has been suggested by Bourne (1957). He considers that the upright position in the dental chair coupled with some degree of anoxia may lead to an unrecognized fainting attack. The conscious patient does occasionally faint or feel faint in the chair, but under nitrous oxide anæsthesia many anæsthetists consider that the blood pressure tends to rise rather than fall. In my experience fainting during anæsthesia is rare, or I have failed to recognize it.

The Resistant Adult Patient

So weak is the anæsthetic effect of nitrous oxide that when given to a resistant patient it proves hopeless and dangerous. I can recall every detail of many of my fiascos with unassisted nitrous oxide, for they include such damage as two broken dental chairs, one dental chair overturned, a sterilizer upset and a spittoon wrenched from a unit. A resistant patient is often a mouth-breather, and the older generation of anæsthetists made use of this behaviour by having a marine sponge soaked in ether ready to be placed in the open mouth during induction with nitrous oxide. This technique led to a search for other adjuvants to nitrous oxide to subdue a struggling patient:

(1) *Ethyl chloride.*—From ether on a sponge it was an easy step to spray ethyl chloride on to gauze suitably placed in the mouth. Ethyl chloride had advantages over ether, for it was easily carried, readily available, non-explosive and extremely powerful. I have not used ethyl chloride to subdue a struggling adult since I was called to a dental surgery twenty-five years ago and saw the mortal remains of one who had been so "subdued". I cannot trust my judgment of dosage of ethyl chloride when given to a patient who takes deep gasping breaths during the stage of delirium.

(2) *Vinesthene.*—This safe yet powerful ether is useful if it can be added to the inhaled nitrous oxide-oxygen mixture at the correct moment. When using static machines commonly found in clinics and hospitals divinyl ether may be given with ease from a dripper designed by Goldman or Harris; for the peripatetic anæsthe-

tist, devices have been made by which ampoules of Vinesthene may be broken inside the nitrous oxide reservoir bag: I prefer the simple and fool-proof method of injecting the drug in a syringe through a Mitchell needle inserted into the nose-piece tubing.

(3) *Trichlorethylene.*—The analgesic effects of the vapour of Trilene have long been used to smooth out the uncertain effects of nitrous oxide. After the absorption of a small quantity of the vapour, a patient may be held in a tranquil state with adequate oxygen in the nitrous oxide mixture. I do not consider Trilene a safe drug when used to control a cyanosed struggling patient. A myocardium whose action is impaired by oxygen lack may not withstand the irregularities of cardiac rhythm caused by the drug. At one time I was disappointed with the after-effects of Trilene as an adjuvant to nitrous oxide, for the patients were drowsy, sluggish and felt unwell. Credit is due to Boston (1956) for showing that such results are due to the use of an unnecessarily strong vapour: by his modification of the variable slot on a vaporizer he can obtain low concentrations of the agent.

(4) *Cyclopropane.*—After more than twenty years' experience with cyclopropane as an anæsthetic, the question may be asked why the gas is not more commonly used to augment nitrous oxide, or why it has not replaced it in dental anæsthesia. Cyclopropane has two drawbacks when used at the chairside. The first is that a disappointingly large number of patients feel sick or are sick. After cyclopropane anæsthesia the patient may comment, "I've never felt like this after gas before". The second objection to cyclopropane is the risk of an explosion. The low energy of the spark required to cause ignition and the multiple potential sources of detonation at the chairside make the explosion hazard difficult to overcome. Cyclopropane contained in a bag with oxygen diluted with nitrogen will not explode, but anæsthesia produced by the inhalation of the contents of a closed bag resembles that of the old "straight gas" in that there is no provision for maintenance.

Intravenous Anæsthesia

I have used intravenous barbiturates for selected patients in the upright position in the dental chair for the past twenty-six years, and the untoward events which have followed this practice have not been sufficiently serious or frequent to make me question whether it is wise or justified. In spite of my enthusiasm for the technique, I use it in only 15% of cases in private practice. Thiopentone anæsthesia has solved the problem of what method to use for three groups of difficult patients:

(1) *Resistant adults.*—It is noteworthy that many resistant patients are intellectual and co-operative. My attempts to subdue their mental activity and render them unconscious with inhalation anæsthesia are often distressing and dangerous. By the use of intravenous anæsthesia, the admitted alcoholic is spared the risks to life and limbs which were certainly present when fighting under nitrous oxide.

(2) *Patients who are intolerant of inhalation anæsthesia.*—Some adult patients find it impossible to retain their self-control sufficiently long to lose consciousness with an inhalation anæsthetic. Towards the end of induction they cannot resist the impulse to tear the nose-piece and tubing from their face, and hold it at arm's length. Often such patients are pathetically apologetic for their behaviour, and I recall a man who pleaded with tears in his eyes that after two failures I should make a third attempt with nitrous oxide. For such patients a rapid injection of a small dose of thiopentone is a revelation in the ease by which consciousness may be lost.

(3) *Patients with cardio-respiratory insufficiency.*—The progress of thoracic and cardiac surgery has given rise to a group of patients who have undergone lobectomy, pneumonectomy or operations for the relief of congenital or acquired heart disease. I consider that it is unwise to expose such patients to the risks of anoxia which may be associated with nitrous oxide anæsthesia. By the use of intravenous thiopentone and nasal oxygen a patient with three-quarters of one lung only has been repeatedly treated in the dental chair with safety.

Old age is no contra-indication to the use of intravenous anæsthesia, but for the octogenarian it is wise to approach with a syringe containing 250 mg. only of thiopentone fitted with a 22-gauge needle, and thus limit the possible total dose and the speed of injection.

The Drawbacks of Intravenous Anæsthesia

The barbiturates are poor analgesics, and therefore more than a hypnotic dose must be given if the patient is not to feel and respond to pain. It is difficult to judge the dose of intravenous thiopentone which will provide tranquil anæsthesia during the time required to complete the extractions, yet not cause profound respiratory depression and an unduly long recovery period. The hazards of the technique are seen particularly

during the stage of respiratory depression and of returning consciousness.

The onset of laryngeal spasm is an ever-present threat to a good airway. During the injection of thiopentone saliva may tickle the throat and cause a cough. The dislodged mucus from the trachea or bronchi irritates the vocal cords and spasm develops. While the extractions are in progress, a trace of blood eluding the throat-pack can have the same result. I have a clinical impression that atropine given with the intravenous barbiturate diminishes the incidence, but by no means eliminates the risk of onset of laryngeal spasm. In my experience the signs of developing spasm are recognized in 1 in 100 cases, and I have learned from many anxious moments how important it is to coax oxygen past the closing cords at the first crowing sound.

After intravenous anæsthesia the time required by the patient to regain a rational state may vary from five minutes to five hours. I can recall a woman who winked at me after 400 mg. of thiopentone and enjoyed a post-extraction cigarette within three minutes of the injection. A woman of similar build was given 500 mg. of thiopentone at 12 noon, but so delayed was her return of co-operation that the advisibility of a bed in a near-by nursing home was mooted. After barbiturate anæsthesia an intravenous injection of nikethamide or bemegride (Megimide) appears to cause wakefulness, but it is doubtful whether the use of either drug substantially shortens the total recovery period.

A rare but distressing result of intravenous thiopentone is a patient affected with a short bout of mania or hysteria. In this state commands are not obeyed, and physical restraint may be required to prevent a struggling patient from injuring himself. My notes on the worst example of this behaviour state that "two straps and two chaps" were necessary to immobilize the patient in the chair.

Ultra-short-acting Barbiturates.—Buthalitone (Baytenal) given by intravenous injection produces loss of consciousness with ease and comfort, but the anæsthetic effect is so transitory that nasal nitrous oxide must be given before extractions are attempted. The use of buthalitone may sacrifice tranquil operating conditions for the sake of a rapid return to consciousness, and is therefore not the drug of choice for the difficult extraction or for the difficult patient. Organe finds the length of anæsthesia and the period of recovery of a patient given a large dose of buthalitone indistinguishable from that produced by a small dose of thiopentone.

Intravenous pethidine.—The analgesic effect of pethidine can be used as a valuable supplement to nitrous oxide anæsthesia. If an intravenous injection of 25–50 mg. of pethidine is given five minutes before nitrous oxide anæsthesia is induced, it will be found that the patient does not respond to painful stimuli although the oxygen content of the maintenance mixture of nitrous oxide is high. In the doses suggested, pethidine does not prolong the recovery period, neither does it produce any unpleasant subjective sensations. Another use of intravenous pethidine is to augment the effects of local analgesia in the mouth—the result is wholly satisfactory but beyond the scope of this discussion. In my experience intravenous pethidine is a safe and useful drug, and it is comforting to know that in the event of a relative overdose being given, Galley (1959) has confirmed that a reliable antagonist nalorphine (Lethidrone) is available.

The Hazards of Minor Oral Surgery

Anæsthetists are sometimes asked to provide time and tranquillity at the chairside for dental operations of such duration and difficulty as are commonly performed in an operating theatre.

A dental surgeon decided to remove an impacted lower 3rd molar tooth from a tall Irish Master of Foxhounds. The patient was given 500 mg. of thiopentone intravenously followed by nasal nitrous oxide. He was quiet and still for two minutes. At a later date in a nursing home under endotracheal anæsthesia the tooth required three-quarters of an hour's operating time for its removal.

The work of Brock (1947) is a warning to dental surgeons and anæsthetists. He showed that when the ætiology of lung abscess is investigated, 25% of cases have a history of multiple extractions under general anæsthesia in the dental chair. During nitrous oxide or intravenous anæsthesia the efficiency of the throat pack may be sacrificed to the maintenance of a good airway. Many anæsthetists feel that if the time required for the extractions is likely to exceed seven minutes, the only way to keep a good airway with a satisfactory throat pack is by means of an endotracheal tube. An ingenious method which avoids the use of an endotracheal tube and throat pack is to place the patient in a steep head-down position in the dental chair. So unusual is the posture, however, that few dental surgeons have sufficient hypnotic influence over their patients to retain their co-operation during a worm's eye view of the adjustment of restraining straps and other devices which are necessary to prevent the head and trunk from sliding to the floor.

REFERENCES

BOSTON, F. K. (1956) *Anæsthesia*, **11**, 37.
BOURNE, J. G. (1957) *Lancet*, ii, 499.
BROCK, R. C. (1947) *Guy's Hosp. Rep.*, **96**, 141.
DAWKINS, C. J. M. (1958) *Brit. med. J.*, i, 1116.
GALLEY, A. H. (1959) *Anæsthesia*, **14**, 82.
GOULDING, R., HELLIWELL, P. J., KERR, A. C., and WILKIN, E. M. (1957) *Brit. med. J.*, i, 855.
GRAY, T. C., and HALTON, J. (1951) *Int. dent. J.*, **1**, 25.
Lancet (1934), i, 154.
MOSTERT, J. W. (1958) *Brit. med. J.*, i, 502.
TOM, A. (1956) *Brit. med. J.*, i, 1085.

DISCUSSION

Dr. J. G. Bourne: Interest in dental anæsthesia has recently been renewed. This is to be encouraged. Dental anæsthesia merits attention because, in England and Wales alone, more than two million administrations are given annually. The nitrous-oxide method is used in at least three-quarters of the cases and has now been in use in this country for ninety years; yet surprisingly little is known about its sequels.

To give nitrous oxide to patients sitting up in the dental chair has always been considered safe. But in a recent inquiry I found that severe cerebral sequels were common. The evidence I collected left me in no doubt that their main cause was fainting (Bourne, 1957, *Lancet*, ii, 499). A common fainting attack occurred while the gas was actually being given; it was therefore masked by the anæsthesia and was overlooked. As a result, the patient was kept upright and consequently was liable to be without any cerebral circulation whatever while the extractions were being made. His brain was in the same danger as if his heart had stopped beating.

Dr. McConnell has told us that he meets with cases of delayed recovery once or twice a year, or once in every 1,000 or 2,000 cases. This is consistent with my findings that delayed recovery occurs even with the most experienced and skilful dental anæsthetist and that it has an incidence of at least 500 cases a year in the United Kingdom. He differs from me, however, in thinking that its usual cause is anoxic anoxia. He says that he has never recognized a fainting attack during the administration of gas. This is very likely; but it is not to say that fainting has never occurred under his hand. My whole point is that fainting under gas escapes recognition and has persisted in doing so all these many years. It is interesting to note that, ninety years ago, in the discussion following presentation of the very first report in this country on the use of nitrous oxide in dentistry, when about 2,000 administrations were reviewed, two speakers described cases of delayed recovery. A girl, aged 11, was in stupor for twenty minutes; and another, aged 17, "remained in the operating room for half an hour in a state of partial unconsciousness very like that produced by poisoning with opium" (*Trans. Odont. Soc., Lond.*, 1869, N.S. **1**, 31). She was sent home in a carriage with attendants while still in a state of stupor. We may ask to-day how many tens of thousands of patients since then have been sent home in stupor, and how many brains have been damaged.

Dentists and dental anæsthetists should be warned of the danger of fainting under gas. They should be on the look-out for its signs: pallor, sweating, irregularity or cessation of respiration, twitching of muscles, dilatation of the pupils and a pulse that is absent, or else feeble and, as a rule, slow. If any one of these appears, work should stop immediately and the patient should be laid down in the horizontal position without a moment's delay. Oxygen and artificial respiration should not be given until the patient is horizontal.

Dr. V. Goldman commented that he had heard of one explosion which had occurred with Vinesthene in dental work and this had been reported in America (Seldin, 1958). He went on to say that he himself had had very little success in difficult cases with the technique of amnalgesia in adults as described by Klock (1955). He had discussed the technique with Dr. Klock, who was understood to say that in long or difficult cases after the stage of amnalgesia had been reached he frequently injected some form of local analgesic in order to help him with his extractions.

Finally Dr. Goldman asked Dr. McConnell about those cases which he had stated occurred about twice a year and in which there had been some delay in recovery or the patient had been apparently somewhat ill after the administration of an anæsthetic; he would like to know whether such cases were those which showed some indication that they might have been suffering from the type of fainting or drop in blood pressure described by Dr. Bourne, or whether they occurred when Dr. McConnell might have been pushing the gas rather more than was advisable; or if he felt that in the cases concerned the airway might have been impaired. He felt that an answer to this question would be of considerable value coming from such a master of the technique as Dr. McConnell because in his own experience it was always when one had done something one should really not have done that these difficulties and delayed recoveries occurred, and not that there had been a fainting attack or drop in blood pressure in the patient, during the administration.

REFERENCES

KLOCK, J. H. (1955) *Curr. Res. Anesth.*, **34**, 379.
SELDIN, H. M. (1958) *J. Amer. dent. Soc. Anesthesiol.*, **5**, 5.

Dr. F. R. Gusterson commended Dr. Mostert's method of administering nitrous oxide especially in the frail or elderly patient in whom even transient anoxia could be dangerous. If during the preliminary administration of the oxygen it was explained to the patient that this was done to ease the breathing, patients did not often complain of the time taken to lose consciousness.

The discussion had emphasized the dangers of any degree of anoxia during dental anæsthesia. He felt that when an anæsthetist was confronted with a resistant and unpremedicated patient in the dental

chair and could not obtain the necessary state of anæsthesia without anoxia, his greatest service to both the patient and the dentist was to refuse to continue the administration.

Dr. J. N. Fell said that there was no reason why in chairside dental work anæsthesia should not be induced with nitrous oxide and a small percentage of oxygen, up to 10%, instead of the usual pure nitrous oxide as practised by Dr. McConnell, provided that one had a good machine and a co-operative patient. Although the induction time was a little longer, there was less likelihood of trouble resulting from anoxia or asphyxia.

Dr. C. J. Massey Dawkins suggested that if an intravenous barbiturate was administered to a patient in the dental chair, it would be better to give hexobarbitone rather than thiopentone on the grounds of increased safety, far less likelihood of laryngeal spasm and absence of danger due to inadvertent intra-arterial or perivenous injection. He added a plea to dental surgeons to see, if the patient was a child, that a proper-sized seat was provided so the anæsthetized child could not slide out of it—as would inevitably happen if the child was perched on a cushion in an adult chair.

Dr. W. N. Rollason made the following three points:

(1) Dr. McConnell had mentioned that he only used intravenous anæsthetics in the dental surgery in 15% of cases. Among this 15% he included cases of congenital heart disease. Dr. Rollason asked Dr. McConnell if in fact he would anæsthetize in the dental chair a case of congenital heart disease associated with cyanosis.

(2) Dr. McConnell had referred to troublesome laryngeal spasm occurring in 1 in 100 cases when intravenous Pentothal was used in the dental chair. Dr. Rollason had never seen a case of troublesome spasm in several thousand cases induced in the dental surgery provided Pentothal was limited to 25 mg./stone body weight. This was followed by nitrous oxide and oxygen for maintenance, and in the resistant subject ethyl chloride was sprayed on the oral pack in addition. Provided the ethyl chloride was used only when the patient was breathing and had a reasonable airway it had proved safe and effective and no explosion had occurred.

(3) He felt a case could be made out for routine intubation under direct vision in the dental surgery but this required the services of a specialist anæsthetist and appropriate equipment.

The President asked Dr. McConnell (1) if he had any actual figures relating to the incidence of vomiting after dental gas, and (2) if he considered that the explosion hazard was not also present when Vinesthene was used.

Dr. Frances Sorrell asked Dr. McConnell's opinion on outpatient dental gases for pregnant women with special reference to the type of case where the patient was nervous but her home conditions made sedation difficult.

Dr. W. S. McConnell, in reply to Dr. Bourne, said he attributed any incident which led to anoxia and resulted in delayed recovery of consciousness to some error on his part, rather than to a faint.

In answer to Dr. Goldman he agreed that in untoward incidents during nitrous oxide anæsthesia the emergency was more commonly precipitated by some error on the part of the anæsthetist as opposed to a faint by the patient. He hoped that with increased experience and acuity of observation he would meet with such cases even less frequently in the future.

Dr. Gusterson had stressed an important duty of the anæsthetist: if safe and tranquil anæsthesia cannot be obtained with nitrous oxide the operation should stop. The patient will give credit to the dental surgeon and anæsthetist for their judgment rather than blame them for failure after a truthful explanation is given.

Dr. Fell advocated inducing patients with oxygen and nitrous oxide. Dr. McConnell agreed that with a co-operative patient any slow induction technique was possible, but the method might fail in those with limited self-control.

Dr. Massey Dawkins preferred hexobarbitone to thiopentone for three good reasons. Dr. McConnell considered that the occasional sneezing, coughing and movements during the injection of hexobarbitone together with a more prolonged recovery period for a given depth of anæsthesia outweighed the suggested advantages.

In reply to Dr. Rollason, he did not advise chairside anæsthesia for children with congenital heart disease. He suggested that all such cases should be treated in hospital in the first instance and only after a satisfactory assessment of cardiac reserve should the child be given an anæsthetic in the dental chair.

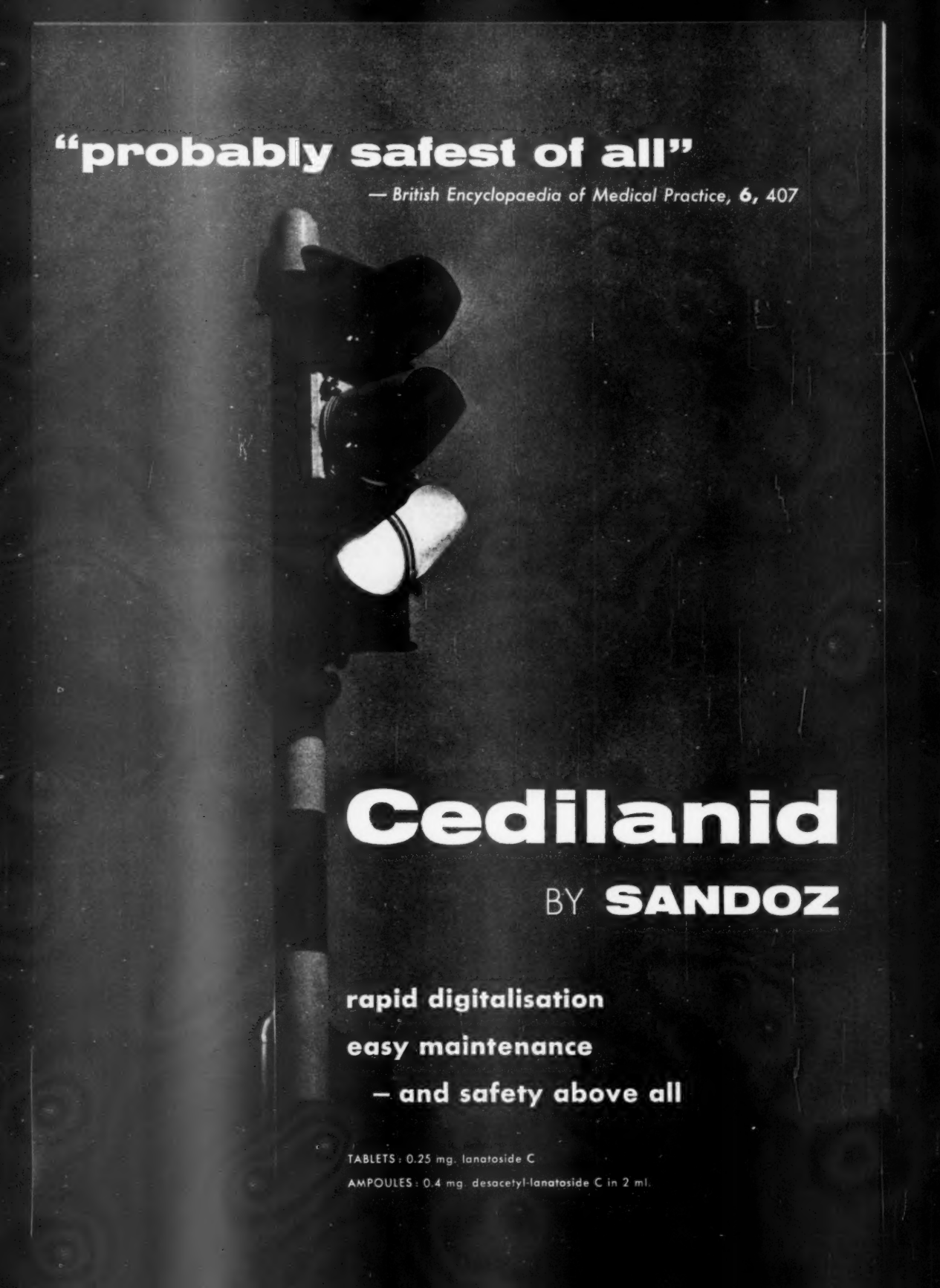
Routine intubation of patients in the dental chair could be justified only if all dental extractions were prolonged. It would seem unwise and unnecessary to add the risk of injury from intubation for a short procedure.

Dr. McConnell could not agree that the threat of laryngeal spasm was excluded by the routine use of a small dose of thiopentone; in his experience it could occur whether the dose was large or small.

In answer to the President, he regretted he had no secret which would prevent a patient vomiting after a somewhat prolonged nitrous oxide anæsthetic.

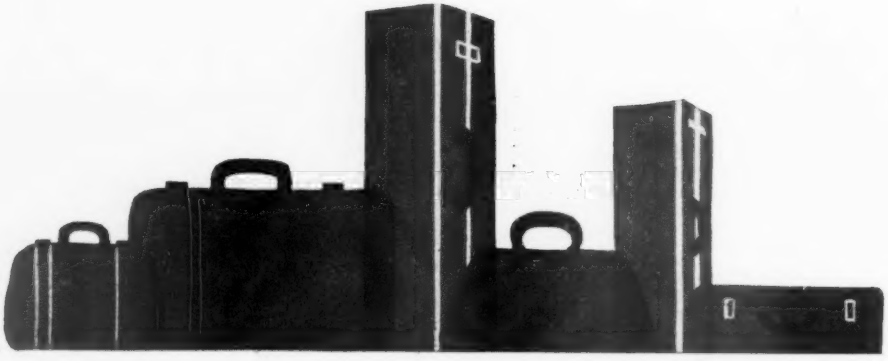
He was grateful for the timely reminders about the explosion risk when divinyl ether was used.

In reply to Dr. Sorrell about the management of nervous pregnant women, the speaker said that in his experience such patients could be given nitrous oxide and oxygen at any stage of the pregnancy.


"probably safest of all"
— British Encyclopaedia of Medical Practice, 6, 407
Cedilanid
BY SANDOZ
rapid digitalisation
easy maintenance
– and safety above all
TABLETS: 0.25 mg. lanatoside C
AMPOULES: 0.4 mg. desacetyl-lanatoside C in 2 ml.

Everybody can

travel in comfort



DRAMAMINE

BRAND OF DIMENHYDRINATE

SEARLE

DRA : 49

Proceedings of the Royal Society of Medicine

Vol. 52
331

Section of Radiology

President—B. W. WINDEYER, M.R.C.P., F.R.C.S., F.F.R.

Meeting
October 17, 1958

Some Radiological Aspects of Congenital Anomalies of the Spine in Childhood and Infancy

By JOHN FAWCITT, M.R.C.S., L.R.C.P., D.M.R.(D.)
Manchester

THE responsibility of the radiologist in the assessment of congenital anomalies of the spine starts whilst the infant is still unborn and remains of importance in its evaluation throughout childhood.

Two aspects of the problem will be discussed. The first is that of coronal cleft vertebræ, which is closely bound up with the fœtal and immediate neonatal period. The second, which is the assessment of the incidence and importance of spina bifida of the lower lumbar and sacral spine, extends throughout youth.

CORONAL CLEFT VERTEBRÆ

Coronal cleft vertebræ are being described with increasing frequency as the knowledge of their existence becomes more widely disseminated. It is now discovered not uncommonly in the later stages of pregnancy when lateral views of the fœtal spine may show in one or several of the lumbar or dorsal vertebræ a vertical translucent cleft which is situated more posteriorly than anteriorly. The affected vertebræ tend to appear somewhat larger than those adjoining them. An example is shown in a neonate involving the third and fourth lumbar vertebræ (Fig. 1). Among others, two excellent papers have been written on this anomaly. The first, an extremely authoritative one, was by Rowley (1955) in which 28 cases were described: the embryological background of the condition was discussed and its predominantly male incidence stressed. Follow ups were done on a number to assess their duration after birth.

FIG. 1.—Coronal cleft vertebræ in L.3 and 4 in a normal full-term Swedish baby.

The American paper by Cohen *et al.* (1956) does not give the condition the name of coronal cleft vertebra but describes it as "A significant variation in ossification centres of vertebral bodies". They report the condition as having a frequency of 17 out of 400 patients. They put forward the hypothesis that no one type of ossification pattern exists universally in the formation of the vertebral body. They suggest, however, that though it is a harmless variant, there is a significant increase in its incidence in the presence of other anomalies.

The present material consists of 7 cases obtained over the last eighteen months.

4 of these were discovered and reported in the films of the fœtus. 2 were visible in the lateral serial radiographs of infants at the time of delivery in the 32 cases which I saw when working with Professor Lind in Stockholm; and the seventh was a coincidental finding in an infant of 3 weeks old with an acute respiratory infection.

5 of the cases were males and 2 females.

In 2 of these cases the disappearance of the coronal cleft was observed. The first of them, which was visible at 35 weeks gestation, occurred in the third and fourth lumbar vertebræ, but the film of the infant at birth showed only the ghost of these clefts. In the second case, which was the infant with the acute respiratory infection, only the fourth lumbar vertebra (Fig. 2) showed a coronal cleft in a rather large vertebral body; six

weeks later a further radiograph showed only the ghost of the cleft (Fig. 3).

One of the cases which was observed before birth showed an unusual anomaly of the coronal clefts in the fourth and fifth lumbar vertebræ where there appeared to be some displacement of the anterior segment of the fifth lumbar with anterior loss of disc space of the fourth and fifth lumbar vertebræ. The infant was clinically normal and unfortunately it has not so far been possible to obtain further radiographs.

This condition has been discussed with Dr. Blair Hartley, who has observed approximately 80 cases of coronal cleft vertebræ. He confirms that the value of observing it is the negative one of being able to reassure the obstetrician that it is an anatomical variant, rather than a pathological finding.

FIG. 2.—Coronal cleft vertebra in L.4 in an infant of 11 days of age.

FIG. 3.—Disappearance of the coronal cleft six weeks later with some residual enlargement of L.4.

SPINA BIFIDA

Only one statistical review of the incidence of spina bifida with major emphasis on childhood and infancy has been discovered in a search through the cumulative medical index for the past fifteen years. Sutow and Pryde (1956) assessed the frequency of spina bifida in 540 Japanese in four age groups, 155 in the 7- to 8-year-olds: 95 12-year-olds: 108 16- to 18-year-olds: and 182 adults. From their figures there was a steady diminution in its incidence through the age groups from 58·3% in the youngest to 28·5% in the adults, with a marked overall preponderance of the bifid lesion in the first sacral vertebra.

In the absence of a large scale review of spina bifida in childhood of recent years, an analysis was made of the radiographs of the last 500 children at Booth Hall Children's Hospital, Manchester, showing the lower lumbar and sacral spines. The cases were consecutive and unselected except for the exclusion from the series of cases of meningocele and meningomyelocele with gross spinal anomalies. In this series, spina bifida occulta has been taken to mean incomplete closure by ossification of the laminæ of any of the lumbar or upper sacral vertebræ radiographed.

Of these 500 cases, 410 (82%) have shown some element of spina bifida occulta of varying degree. These figures have been subdivided into age groups of 0–5 years, 6–10 years and 11–16 years. In the first quinquennium in which 191 infants were radiographed 179 (94%) had spina bifida. In the second period 213 cases were examined and 74% had spina bifida, whilst in the third five-year period 96 examinations including the lumbar or lumbo-sacral area were performed and 72 or 75% showed the spina bifida.

It is noteworthy that the percentage of spina bifida did not materially change in the two later age groups and that it remained as high as 75%. As was to be expected the percentage dropped steeply after the first quinquennium as ossification of the spinous processes takes place about that period, though Caffey states that the two bony centres of the arch extend posteriorly towards the mid-line and complete the bony neural arch in the first two post-natal years. These figures for spina bifida occulta are far higher than those given in 1950 by Southworth and Bersack for 550 adults whose lumbo-sacral areas they examined and who showed only 18·6% spina bifida; whilst Brailsford's (1953) analysis of 3,000 spines gave the incidence of spina bifida occulta of L.5 as 6% and S.1 and 2 as 11%; a total of 16% overall.

The distribution of the spina bifida was examined in the same age groups previously used (Table I). As would be expected 54% of the

TABLE I.—DISTRIBUTION OF SPINA BIFIDA

Site	Total	0–5 years	6–10 years	11–16 years
L.5	23	15	4	4
S.1	270	93	118	59
L.5 and S.1	80	52	24	4
S.1 and 2	13	7	6	—
S.2	1	—	—	1
Others	23	12	7	4
Nil	90	12	54	24
Totals	500	191	213	96

total were at the first sacral level and if two of the other categories are included—those of L.5, S.1 and S.1 and 2 the total is 72·6%.

A further review of the figures into the causes for which the examination was made showed that 237 (49 without spina bifida) were for straight films of the abdomen taken because of abdominal pain, foreign bodies, &c., 107 examinations were for lesions of the hip-joints, and 102 were for urinary investigations including 13 for enuresis in which 2 cases showed no spina bifida. The final group was examination of the spine for a variety of reasons including pain in the back, spondylolisthesis, suspected tuberculosis and a few for the identification of spina bifida or spinal anomalies in congenital lesions of the lower limbs. Of these last, 54 cases were radiographed of which 8 had no spina bifida. The frequency of spina bifida was also assessed in 35 cases of congenital dislocation or subluxation of the hip. Of these, 29 had spina bifida and in addition there were 3 cases with gross spinal anomalies, whilst only 4 were free of spina bifida.

An attempt was made, in addition, to analyse the figures showing the frequency of spina bifida in children with congenital anomalies of the lower limbs. It was found, however, that there was not a high enough proportion of radiographs of the spine in these cases to make the investigation statistically reliable.

This analysis of spina bifida in infancy and childhood suggests that, even allowing for the expected high figure of 94% in the first quinquennium when the laminæ of the lumbar and sacral areas have not completely ossified, spina bifida occulta of the lower lumbar spine or sacrum is not a significant finding by itself.

In the light of examination of the spines of a large number of children with congenital anomalies a general dictum is suggested for which, however, there is no proven statistical support but which the author believes to be generally true.

In broad terms, the cervical spine tends to show errors of segmentation with fusion, as in the case of the relatively common Klippel-Feil deformity. Hemivertebræ are most usually seen in the dorsal spine; the lumbar spine and upper sacrum are most commonly associated with spina bifida of varying degrees of severity; whilst abnormalities of the sacrum are most usually those of hypoplasia or aplasia which are generally associated with disturbance of the urinary tract.

It should be stressed, however, that spina bifida in childhood ought not to pass unreported by the radiologist, particularly in cases of congenital anomalies of the lower limbs, and occasionally, and more commonly than is perhaps realised, diastematomyelia may be discovered.

Acknowledgments.—I would like gratefully to acknowledge the help of Mr. L. Cunliffe, the schoolmaster at Booth Hall Hospital, in the preparation of Table I, and of Miss J. Perry, Medical Artist of Crumpsall Hospital, in making the illustrations.

REFERENCES

BRAILSFORD, J. F. (1953) The Radiology of Bones and Joints. 5th ed. London; p. 400.
COHEN, J., CURRARINO, G., and NEUHAUSER, E. B. D. (1956) *Amer. J. Roentgenol.*, **76**, 469.
ROWLEY, K. A. (1955) *J. Fac. Radiol., Lond.*, **6**, 267.
SOUTHWORTH, J. D., and BERSACK, S. R. (1950) *Amer. J. Roentgenol.*, **64**, 624.
SUTOW, W. W., and PRYDE, A. W. (1956) *Amer. J. Dis. Child.*, **91**, 211.

Observations on Spinal Tumours in Childhood [*Abridged*]

By KENNETH TILL, F.R.C.S.
London

IN this short communication I present some observations upon a small series of patients up to the age of 12 years who proved to have tumours within the spinal canal. Such lesions are fortunately rare in children although neoplasms in this age group occur more often in the central nervous system than elsewhere in the body apart from the lymphoid system. To give a true sense of proportion concerning the incidence of this disease group, I would mention that during the five-year period 1953–58 there were admitted to the Department of Neurosurgery at The Hospital for Sick Children, Great Ormond Street, London, 1,300 patients; of these 214 (16%) were suffering from tumours in the central nervous system. Of these 214 tumour cases only 28 occurred in the spinal canal, i.e. 2% of the total admissions. These cases are summarized in Table I.

TABLE I.—28 CASES OF SPINAL TUMOUR IN CHILDREN 1953–58

(*Under 13 Years of Age*)			
Neuroblastoma	7	Ganglioneuroma ..	1
Arachnoid cyst	3	Astrocytoma	1
Ependymoma	2	Extradural sarcoma ..	1
Neurofibroma . ..	2	Intramedullary abscess	1
Dermoid cyst	2	Hamartoma	1
Unverified intramedullary	4	Diastematomyelia ..	3

I have excluded those cases in which the spinal

lesion was secondary to an intracranial tumour. The series will be seen to contain several cases which are not strictly neoplastic. The arachnoid cysts, the rare intramedullary abscess and the diastematomyelia are included because they may present clinically like a tumour and are not always capable of differentiation from true spinal neoplasms on clinical and radiological grounds. The distribution of cases in groups shown in Table I does not resemble the series which have been published (Ingraham and Matson, 1954). This is merely a reflection of the paucity of cases in any one department so that chance has included an intramedullary abscess but excluded many other possible diagnoses such as lipoma, medulloblastoma, teratoma, chordoma and hæmangioma.

It has been justly said that there is probably no other neurosurgical condition in which the history is so apt to be inadequate and in which there may be such a lack of signs early in the disease. There are two principal difficulties peculiar to this age group. Firstly pain is an infrequent symptom since the meninges and nerve roots are less often involved than they are in adult life. (When pain does occur it may be impossible in a young child to determine its exact site or the presence of radiation due to nerve root compression.) Secondly, the testing for sensory loss which is such a valuable aid in the older patient is often unreliable despite the most painstaking examination.

The symptoms and signs which have occurred in this series are as follows: motor weakness, muscle wasting, sensory loss, paræsthesiæ, backache, back stiffness, alteration of spinal curvature, abnormality of gait, constipation, abdominal pain, frequency or retention of urine, shortening of one leg and talipes. The diagnostic difficulty is that only one symptom or sign may be present for many months or even years before fresh signs develop. Such solitary complaints which have proved in retrospect to be due to spinal tumours have included abdominal pain, constipation and frequency of micturition.

It is apparent when reviewing the history of these 28 cases that the wise advice given by Ingraham and Matson (1954) is either unknown or unheeded. They say that "early accurate diagnosis of intraspinal tumour in children implies first realization that such a lesion is a possibility, and second investigation of minimal symptoms and signs by objective diagnostic aids including spine roentgenograms, spinal fluid study, and contrast myelography". The following two cases illustrate the worth of this advice.

Case I.—Girl, aged 5 years. When aged 18 months, after an attack of whooping-cough she was found to be unable to bend her back normally. She appeared to have pain in the back occasionally. At the age of 2½ years she had been admitted to an orthopædic hospital suspected of suffering from spinal tuberculosis. The X-rays were said to show no abnormality and there were no abnormal physical signs apart from a stiff back. She was treated successively on a frame and in plaster without effect and was eventually considered to have a "functional nervous disorder". When first seen in the Neurosurgical Department at the age of 5 years she had a rigid lumbar thoracic spine with dorsal kyphosis and lumbar lordosis. She had developed no new symptoms and there were no abnormal neurological signs. X-rays showed gross narrowing of the pedicles of L.1 and L.2 and marked widening of the spinal canal in this region (Fig. 1). On lateral view the posterior borders of the vertebral bodies were concave (Fig. 2). We later discovered these appearances on X-rays taken one year previously. There was no difficulty in deciding that a space-occupying lesion was present and myelography, using air as a negative contrast medium introduced by the cisternal route, revealed a complete block at the level of the body of L.1. Forty-eight hours after myelography some air had passed the tumour and outlined its lower border at the level of the body of L.3. At operation a dermoid cyst was found.

It is apparent from this story that had Ingraham and Matson's advice been heeded, namely that the possibility of intraspinal tumour should be remembered and that roentgenogical study must be careful and complete, then an

FIG. 1 (*Case I*).—X-ray of lumbar spine to show widening of spinal canal and thinning of pedicles due to a dermoid cyst.

FIG. 2 (*Case I*).—Lateral view of lumbar spine to show concave posterior borders of vertebral bodies.

unnecessary delay in diagnosis would have been avoided. This tumour was in fact only partially removed since the cyst wall had become firmly adherent to the conus and to the cauda equina. It is at least possible that total removal might have been achieved at an earlier date.

Case II is also a 5-year-old girl. For nine months she had suffered attacks of pain in the buttocks three or four times a day which were usually severe enough to make her scream. She was otherwise in good health. She had been seen by a surgeon three months previously who found a rigid lumbar spine and no other abnormality. The spinal X-rays were then and on later occasions normal. The diagnosis of spinal tuberculosis was presumed and she was treated with a plaster bed without effect. Lumbar puncture at a later date revealed fluid containing 150 mg.% of protein and she was referred to the Neurosurgical Department. Repeated examinations failed to elicit any neurological abnormality but her painful attacks continued. Cisternal air myelography revealed an obstruction of the lower lumbar vertebral body but positive contrast was later used to confirm this (Fig. 3). Laminectomy exposed a tumour intimately involving the nerves of the cauda equina. Removal was impossible. Biopsy was considered unjustifiable since it would certainly have caused neural damage where none had been observed before. The tumour was probably an ependymoma. Following radiotherapy she has remained in fairly good health for the past four years, free from pain, but with some incontinence of urine and fæces. Her myelogram films showed a strange phenomenon previously unknown to us. There could be seen fine drops of contrast medium

FIG. 3 (*Case II*).—Myelogram to show complete block due to intramedullary tumour.

within the vertebral body. The volume of contrast was found to diminish during the screening examination and after twenty-four hours had nearly all disappeared while reappearing in the bone. Presumably the opaque oil entered a vessel which led into the vertebral body.

My purpose in describing these two cases is to emphasize the inescapable fact that tumours can grow to a considerable size in a child's spinal canal and cause long-standing but minimal symptoms without in any way provoking a neural dysfunction or abnormal neurological signs. It behoves us therefore to consider more readily the help which cerebrospinal fluid examination and contrast myelography can give. The objections to injecting opaque oil into the subarachnoid space when the possibility of a spinal tumour is nothing more than a suspicion may be countered by using oxygen instead. Tomography may then provide very satisfactory evidence for or against tumour with practically no ill-effect upon the patient. (Lindgren, 1957).

My final illustration is a reminder that congenital anomalies of the spine and neoplasms may well be associated in the same patient.

Case III.—A baby of 9 months had been born with a tuft of hair over the lower dorsal spine. When aged 7 months she was found to move the left leg less well than the right. It was subsequently noticed that the left foot was smaller than the right. Examination revealed only slight impairment of power in the left lower limb, but the left toes were clawed and the ankle held plantar flexed. X-rays of the spine showed widening of the spinal canal from D.10 to L.2 with an abnormal spur of bone in the mid-line suggestive of

diastematomyelia. Mylography, using Myodil, showed a block at the level of L.1, i.e. two vertebræ below the suspected diastematomyelia. At operation the bony peg was found deep to fused laminæ and spinous processes. Caudal to this lay an oval tumour within the dura intimately connected to nerve roots. This was partially removed and proved to be a hamartoma containing fat and muscle, neural and glial tissue.

In conclusion, the occasional extreme difficulty in diagnosing a spinal tumour in childhood, to which I have referred, renders the radiologist's task one of considerable importance. On his study of the plain X-rays *alone* may depend the first diagnosis of the condition. The careful examination of the pedicles, the measurement of the interpedicular distances, the size of the intravertebral foramina, the contours of the posterior borders of the vertebral bodies, the presence of calcification and of bony pegs all require time-consuming care that will sometimes be very rewarding. The radiologist may well guide the clinician to a far earlier diagnosis than is warranted by clinical examination of the child.

Acknowledgments.—I am greatly indebted to Mr. Wylie McKissock into whose department these children were admitted, and to Dr. R. D. Hoare, the neuro-radiologist who carried out the radiological investigations at The Hospital for Sick Children.

REFERENCES

INGRAHAM, F. D., and MATSON, D. D. (1954) Neurosurgery of Infancy and Childhood. Springfield, Ill.

LINDGREN, E. (1957) *Acta radiol., Stockh.*, Suppl. 151.

Papers on **Atlas Stenosis** and **Diastematomyelia** were read by Dr. H. A. MASLOWSKI (Manchester).

Meeting
November 21, 1958

DISCUSSION ON TESTICULAR TUMOURS

Mr. Arthur Jacobs (Glasgow):

In introducing this discussion on testicular tumours I shall try to outline the overall clinical approach to the disease and to indicate pertinent questions at issue on treatment.

Of all malignant lesions encountered in the male less than 1% are tumours of the testis. It has been estimated that in England, Scotland and Wales, there are somewhat over 350 new cases each year, of whom some 6% are first seen at Service hospitals. The average age at onset is around 30 years, though infants and older age groups may be affected. In most reported series, from 12 to 15% have occurred in undescended or maldescended testes or in testes which have been brought into the scrotum. The incidence of malignant transformation in undescended testes is a debatable topic but that it is higher than in normally descended testes would seem to have been statistically confirmed. Gordon-Taylor and Till (1938) found an undescended testis to be the site of new growth in no less than 30% of their series. Because the right testis is more often cryptorchid than the left the incidence of tumour in a cryptorchid testis is higher on the right side, but in normally descended testes there would appear to be no predilection of the tumour for either side.

Symptoms.—Changes in size and consistency of the organ sometimes associated with an ache are the only early symptoms. Occasionally initial symptoms arise from metastasis, secondary to a small tumour unobserved by the patient and scarcely palpable even on skilful examination. Retroperitoneal glands may give rise to a lumbar ache; a mass in the supraclavicular area due to metastatic nodes there can be a first sign. Primary pulmonary symptoms may occur from mediastinal or lung metastasis. Mammary enlargement due to hormonal elaboration by the tumour or to alterations in pituitary function is a rare occurrence. Tumours developing in intra-abdominal testes become manifest by evidence of an enlarging lower abdominal mass; their recognition is therefore usually late. Lesions in testes within the inguinal canal or in an ectopic position external to the ring are usually noted earlier because the swelling is more likely to be felt or traumatized.

Diagnosis.—In considering the diagnosis of a swelling within the scrotum, hydrocele, epididymitis, torsion and trauma have to be differentiated from tumour. A gumma rarely comes up for diagnosis these days.

Hydrocele is quite frequently present in association with tumour. If the aspirated fluid is darkly bloody, this is very suggestive of tumour; when palpation after withdrawal of such fluid reveals a nodular, firm or heavy testis, it almost certainly contains tumour. Epididymitis is usually obvious because of pain, fever, and tender enlargement of the epididymis. A tuberculous epididymitis is firm and nodular but seldom tender. Rectal examination will almost

invariably reveal evidence of a coincidental involvement of the seminal vesicle or prostate or of both these structures and urography will frequently demonstrate a renal focus. Previous tuberculous disease may, however, obscure the diagnosis as with one patient found to have a testicular tumour, who was referred because of a suspected tuberculous epididymo-orchitis when a scrotal swelling appeared whilst he was still under treatment for a pulmonary lesion. Another patient on whom Borthwick (1958) performed epididymectomy for a persisting tuberculous focus developed a tumour in the opposite testis several years later. Epididymal cancer, though rare, may have to be considered when the epididymis contains a firm non-tender swelling.

The clinical recognition of testicular tumours is thus a matter of exclusion and any testicular swelling involving the body alone should be regarded as neoplastic. If a diagnosis cannot be made by external examination, the testis should be inspected after delivery from the scrotum through an inguinal incision and occlusion of the cord with a rubber covered clamp. An example where this was necessary was that of a patient who had a minute solitary intra-testicular nodule only just palpable under the tunica even after the surgical exposure. This proved to be a seminoma. The patient died with widespread metastases a year after orchidectomy and subsequent X-ray therapy.

After diagnosis of a testicular tumour palpation of the inguinal, iliac, and supraclavicular areas should be made for evidence of superficial gland involvement. A chest X-ray to determine the presence or absence of pulmonary or mediastinal metastasis must be routine. X-rays of the long bones, pelvis, and dorsolumbar vertebræ will give further help in the search for metastasis. Intravenous urography may be of value by delineating an upper urinary tract displaced or distorted by retroperitoneal glands. The breasts should be examined for signs of gynæcomastia. It is also recommended that a twenty-four-hour urine specimen should be quantitatively examined for 17-ketosteroids, 17-ketogenic steroids, follicle-stimulating hormone, and chorionic gonadotrophin. If strongly positive, repeated tests during and after treatment may aid in determining the effectiveness of the therapy adopted.

Pathology.—The pathology of testicular tumours will be discussed by Dr. Thackray. It is essential to co-ordinate the categories so that assessments of the efficiency of different treatments will be based on a comparison of tumours with similar pathology. It is known that the outlook following adequate treatment of a pure seminoma is relatively good whilst that for choriocarcinoma is almost hopeless. Prognosis must be based on the most malignant component present.

Spread.—Local extension to adjacent tissues is of little consequence in this disease for the lesion tends to remain well confined. Lymphatic metastasis is the important route of dissemination and the lymph nodes most commonly affected are those related to the iliac vessels, the aorta and the inferior vena cava. The essential features of testicular lymph drainage according to Hutchison (1958), who has an especial interest in applied anatomy, are as follows: (*a*) The main drainage is directly to the para-aortic nodes of the lumbar region. (*b*) Some lymphatics drain to the nodes on the lateral aspects of the common iliacs. (*c*) There is free communication between the lymphatics of the two sides. (*d*) There is free communication between lymph nodes at the origin of the renal vessels on each side. (*e*) The abdominal lymphatics anastomose freely with the para-aortic lymph system in the thorax and these in turn with the cervical nodes. It is usually stated that the inferiorly situated nodes are affected first. It has, however, been shown (Cooper *et al.*, 1950) that, because the efferent lymphatic channels from the body of the testis pass with the spermatic vessels through the inguinal canal to the lumbar lymphatic area above the iliac level, the renal pedicle nodes are often the primary site of metastasis. The nodes in the region of the iliac vessels normally receive the lymphatic channels from the epididymis. Their involvement, as well as contralateral spread to the opposite side, according to Cooper *et al.* (1950) occurs subsequent to mechanical blockage of the lymphatic channels by tumour emboli.

Hæmatogenous metastasis is usually later and the organs most frequently involved are the liver and lungs, although other organs and tissues of the body may be affected.

The specific incidence of metastasis found by different authors varies; a few examples will suffice to show the significance of spread in this disease. In a series of 250 cases reported by Lewis (1948) 43% had proved metastases on admission and 28% developed them later. In a study of 26 cases at post-mortem, Auerbach *et al.* (1946) recorded retroperitoneal lymph nodes in 92·3%. There was metastasis to the liver in 69·2%; to mediastinal lymph nodes in 80% and involvement of the lung in 84·5%. The more primitive the tumour the greater is the frequency and extensiveness of the spread. This is borne out by the analysis of metastatic sites relative to tumour grouping, which was made by the Armed

Forces Institute of Pathology (Dixon and Moore, 1952). Taking for the purpose of illustration the two groups already mentioned and two sites commonly affected, it was found in 36 autopsies on cases of seminoma that 71% had periaortic and iliac lymph node involvement and 38% lung metastasis; in 7 autopsies on cases of choriocarcinoma the lymph node and lung involvement was 100%.

Treatment and prognosis.—It will be apparent from these facts that any plan for the eradication of testicular tumour disease is inevitably beset with difficulties. Treatment has two divisions: surgery and radiation. Chemical and hormone therapy are not as yet developed to a degree which allows an evaluation of their effectiveness.

There is general agreement that the affected testis should be removed. Orchidectomy is best accomplished through a groin incision above the inguinal ligament and the cord up to near the internal ring is removed along with the testis. This, little more than the provision of a specimen for biopsy, is the accepted role of surgery in this country, the operation being followed by X-ray therapy. A five-year or more survival rate for up to 85% of patients with seminomata, which are very sensitive to radiation, is claimed for this method of combined treatment. For those with tumours of the other groups, which except for a few rare types are highly malignant and radioresistant, 20 to 50% are said to have a chance of a five-year arrest. Figures from the Radiotherapy Department of the Glasgow Royal Infirmary (Morrison, 1958) show that out of 43 cases of all varieties of testicular tumour treated during the years 1940–1953, 14 (13 seminomata and one teratoma) are living, 6 having survived for ten years or more. These 14 are from a group of 25 who had no evidence of metastases at the commencement of treatment. The other 11 died within three years of commencing treatment. Only 1 out of 18 who had confirmed distal spread lived more than five years; the average survival for this group was twenty-two months. In Gordon-Taylor's series (1948), of 155 cases that might have lived ten years, there was a 23·9% survival rate. Leucutia *et al.* (1948) in a study of 110 cases found an overall fifteen-year survival rate in 33%.

In an attempt to obtain improved long-term results some workers advocate more extensive surgery for the large group of tumours which are not pure seminomas. Leadbetter (1958), using a thoraco-abdominal approach, carries out a retroperitoneal lymph node dissection and removes all the tissues from about the aorta or vena cava, depending on the side affected, from the level of the crus of the diaphragm above, to the femoral canal below. If many positive nodes are present, or if enlarged nodes are palpable on the contralateral side, he performs a similar operation after a suitable interval on the side opposite the tumour. At several centres, mostly in the U.S.A., where this type of radical operation is employed, subsequent X-ray therapy may be routine or used only if the excised nodes are found to be positive.

Whether or not this radical surgical approach or improved X-ray therapy resulting from supervoltage apparatus is the more likely to affect results and yield increased survival rates will be shown only after carefully controlled comparative studies and a scientific evaluation of the facts. It is hoped that co-ordination of the work now being carried out by the British Testicular Tumour Panel and Registry with the Clinical Group and by investigators associated with the international research project initiated at the Memorial Hospital, New York, will, with the passage of time, result in an answer to this and other perplexing problems presented by testicular tumours.

REFERENCES

AUERBACH, O., BRINES, O. A., and YAGUDA, A. (1946) *J. Urol.*, **56**, 368.

BORTHWICK, W. (1958) Personal communication.

COOPER, J. F., LEADBETTER, W. F., and CHUTE, R. (1950) *Surg. Gynec. Obstet.*, **90**, 486.

DIXON, F. S., and MOORE, R. A. (1952) Tumors of the Male Sex Organs. Washington.

GORDON-TAYLOR, G. (1948) *In:* Textbook of Genito-Urinary Surgery. Ed.: H. P. Winsbury White. Edinburgh and London; p. 560.

——, and TILL, A. S. (1938) *Brit. J. Urol.*, **10**, 1.

HUTCHISON, J. (1958) Personal communication.

LEADBETTER, W. F. (1958) *Amer. J. Surg.*, **95** 341.

LEUCUTIA, T., EVANS, W. A., and COOK, J. C. (1948) *Radiology*, **51**, 177.

LEWIS, L. C. (1948) *J. Urol.*, **59**, 763.

MORRISON, R. (1958) Personal communication.

Dr. A. C. Thackray (London):

Nomenclature and Classification

Testicular tumours vary widely in their structure and behaviour, and must be grouped into separate categories for discussion of their prognosis and treatment. Some, such as interstitial cell tumours of the testis, are rare and usually benign. Others, such as the various lymphoid and connective tissue tumours, do not differ in behaviour from similar tumours elsewhere, and only the naming and grouping of those tumours which are relatively common and almost always malignant will be considered.

The textbooks agree only in describing the subject as "very confused" and it is difficult to find two books in which the accounts correspond exactly. As an illustration of the difficulties that confront us, the sixth edition of Muir's "Textbook of Pathology" (1951) tells us that "the two most important tumours are (*a*) seminoma and (*b*) teratoma". In the seventh edition (1958) we read "the three most important tumours are (*a*) seminoma, (*b*) embryonal carcinoma and (*c*) teratoma". It will clearly be difficult to compare the results of treatment in a series of malignant testicular tumours divided into two groups, with another series split up into three types. This new category, embryonal carcinoma, is not even mentioned in the earlier editions, though it features in another recent and widely circulated account of these tumours, that by Dixon and Moore (1952). They recognize four main groups, seminoma, embryonal carcinoma, choriocarcinoma and teratoma.

Many more examples could be given of such variation from book to book, for writers of textbooks express their personal views and there is no incentive for them to try and agree with one another. Their views influence pathologists to an extent depending on the circulation of the book and the authority of the writer. But with the urgent desirability of comparing the incidence of the different types of tumour in different parts of the world and of comparing the results of treatment in different countries the time must surely come when there will be an agreed international nomenclature and classification.

The testicular teratoma is a circumscribed tumour made up of a variety of differentiated tissues, and with a correspondingly variegated appearance when cut across. The cysts which are often present may be few and large, lined by columnar or cubical epithelium and separated from one another by predominantly fibrous connective tissue, constituting what is often known as fibrocystic disease of the testicle. More commonly the cysts are smaller and fewer and cartilage and bone form prominent features of the intervening tissue. Such well differentiated teratomas are often present from birth or at least an early age, but in contrast to the teratoma of the ovary it is a well-known and melancholy fact that they are very liable to take on malignant characteristics in early adult life. This change may affect one or more of the tissues present, so that there may be for example chondrosarcomatous, myxosarcomatous and adenocarcinomatous metastases side by side in the lung, or each metastasis may be made up of mingled tissues. Much of the original testicular tumour may still be well differentiated and regular, so that with this strong tendency to malignant change a tumour removed for recent increase in size should not be diagnosed as a benign teratoma on a single section, but only after a very thorough search has failed to reveal signs of malignancy. On the other hand, in a tumour made up for the most part of poorly differentiated malignant tissue it may require a search to find some indication such as a nodule of cartilage to mark the growth out as teratomatous in origin (Fig. 1). Atypical trophoblastic tissue may be present, and if it predominates, as it may to the extent of no other tissues being discoverable, the growth is referred to as choriocarcinoma of the testis. These tumours, which are to be regarded as one-sided developments of malignant teratoma, are rare but highly malignant.

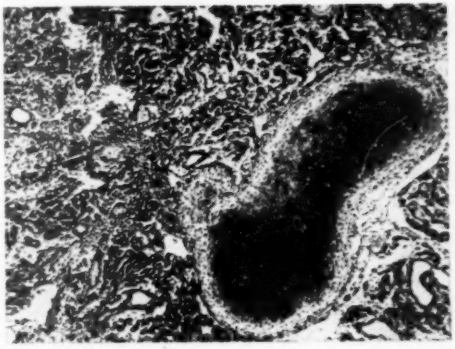


FIG. 1.—Nodule of well-formed cartilage in a malignant teratoma of the testis. × 40.

When a neoplasm of the testis is made up of varied cell types which bear more resemblance

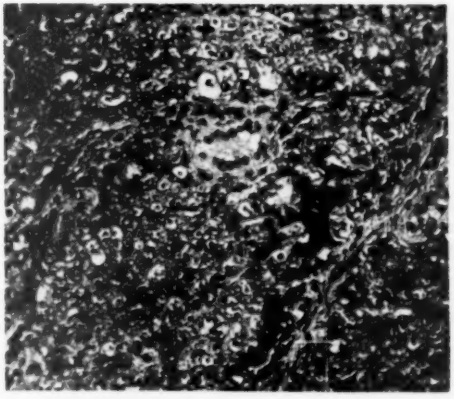


FIG. 2.—Embryonal carcinoma showing an attempt at trophoblastic differentiation. Many mitoses in the sheets of undifferentiated cells. × 155.

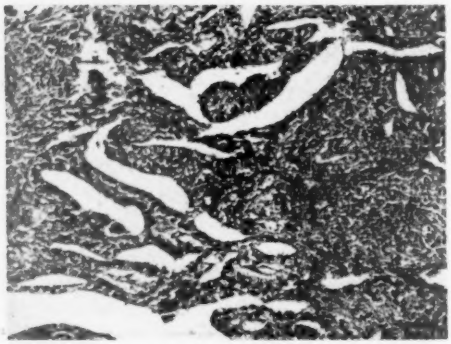


FIG. 3.—Layers of epithelium forming in an embryonal carcinoma. × 70.

to embryonic foetal tissues than to any adult tissue the term embryonal carcinoma is sometimes applied, though as embryonic mesenchyme is often present, carcinoma is hardly the appropriate word. Several different histological patterns are included under this heading. There may be partially successful attempts at differentiation either in the somatic or trophoblastic direction (Figs. 2 and 3), and areas are sometimes seen which are rather fancifully likened to stages in the development of the embryo. As we may find mingled in the same tumour typical so-called embryonal carcinoma and also well-differentiated teratomatous elements, the former might well be regarded as anaplastic malignancy developing in a teratoma. Whatever we call them these tumours are highly malignant, patients only rarely surviving two years.

Although the term embryonal carcinoma has only just appeared among the types of testicular tumour in Muir's "Pathology", the term is not new. It features in Ewing's "Neoplastic Diseases" (1940), for many years a standard work on tumours. He included under this heading a large number of what he described as "embryonal carcinoma with lymphoid stroma". This is clearly what we at present treat as a separate entity, the seminoma. This is the commonest tumour of the testicle, and we regard it as a carcinoma of the germinal epithelial cells of the seminal tubules. It is interesting to note that we are now in line with the beliefs of sixty or seventy years ago. Coats (1895) describes this tumour clearly. "Proper cancer of the testis", he says, "is a large quickly growing soft tumour. . . . The cancerous tissue is derived from the epithelium of the seminal tubules." This view was strongly supported by Chevassu (1906) who called the tumour *séminome*. The intervening years of confusion were due to Ewing's insistence that the tumour was just another sort of one-sided malignant teratoma. It is of practical importance to distinguish this tumour from the quite undifferentiated types of embryonal carcinoma which are so highly malignant and resistant to treatment, because the seminoma, like the spermatogonia and spermatocytes from which it comes, is very radiosensitive.

(Here followed a series of slides illustrating histological variants of seminoma, and also mixtures of the types of testicular tumour described, with emphasis on histological features of prognostic value.)

REFERENCES

CHEVASSU, M. (1906) Tumeurs du Testicule. Paris.
COATS, J. (1895) A Manual of Pathology. 3rd ed. London.
DIXON, F. J., and MOORE, R. A. (1952) Tumors of the Male Sex Organs. Washington.
EWING, J. (1940) Neoplastic Diseases. 4th ed. London.
MUIR, R. (1951, 6th ed.; 1958, 7th ed.). Textbook of Pathology. Revised by D. F. Cappell. London.

Dr. Thomas M. Prossor (London):

The Role of Radiotherapy in the Treatment of Malignant Disease of the Testes

Although this condition is rare no fewer than 580 papers about it have been read or published in the last quarter of a century. The justification for further discussion, I submit, is the ever-present necessity for constant revision and reconsideration of our therapeutic methods in an attempt to improve the control of the disease, and my authority is the study of a series of 318 cases seen at the Westminster Hospital, upon which my remarks are based.

Irradiation was first used in the treatment of malignant disease of the testes by Beclere in 1905 and since then its employment has increased until now its importance overshadows all other therapeutic measures. Opinion in this country has been almost solidly against attempts at a radical operation. In 1947 Gordon-Taylor and Wyndham, having discussed the various forms of treatment, recommended simple orchidectomy and X-ray therapy as the treatment to be preferred, and Cade (1952) said that unquestionably this was the method of choice. In America on the other hand Sauer *et al.* (1948) emphasized the need for reports of cases treated by simple orchidectomy plus irradiation and radical orchidectomy with and without irradiation and, while freely admitting that irradiation should be given in all cases, they recommended that the radical operation still had a place in the treatment of radio-resistant testicular tumours. Lewis (1949) recommended that for teratomas the radical operation be given a fresh trial.

I must point out that his results, 67%, and those of Sauer *et al.* (1948), 48%, although an improvement on Hinman (1933), 17%, are very little better than our own 46% in group 1, and not as good as Professor Windeyer's Middlesex Hospital series stage I teratomas, 74%, quoted by Snelling and Cones (1950).

Whatever the method of treatment employed, consideration of the distribution of the lymphatics from the testes is of paramount importance. In this connexion I make no apologies for quoting again the classical work of Jamieson and Dobson (1910) repeated in 1924 by Handfield-Jones. By injection experiments with prussian blue they showed that the lymphatic vessels from the testes drain not only into the para-aortic nodes, but also that there is a direct communication from the testes to the internal iliac nodes. They have further shown that there is free communication between the primary para-aortic nodes on both sides, which in turn link with the nodes behind and between the two great vessels above and below the renal vessels as well as with the chain along and lateral to the common iliac artery—thus forming what is virtually a large abdominal lymphatic lake. They concluded that the arrangement of the lymphatics of the testes above described is such as to render their complete removal an exceedingly difficult if not impractical procedure. These facts not only explain the reason for the failure of the radical operation, they also dictate the fields to be used in the treatment by post-operative irradiation. The plan for radiotherapy, then, is based upon the distribution of the testicular lymphatics already described but the histological type and clinical extent of the disease has an important bearing on the method to be adopted in each individual case.

The nodes most commonly affected, the para-aortic and internal iliac group, are deeply situated and as there is no certain way of detecting their early involvement it is right to assume that they are affected and to treat them in all cases. In order that these nodes may be irradiated to a satisfactorily high level, treatment is not given to the chest unless metastases are found to be present in the mediastinum.

The presence of intrathoracic metastases, however, makes it necessary to treat the chest in addition to the abdominal nodes, whether or not the latter are palpable. In these circumstances the volume of tissue to be treated becomes very large, and it is always difficult, and sometimes impossible, to deliver an adequate tumour dose to the whole of the affected volume without grave risk of serious blood changes. Nevertheless the radiosensitivity may prove so great that the disease can be controlled for long periods if some method of treatment can be devised. Hitherto the physical factors generally used in the treatment of the lymphatic drainage area of the testes with post-operative high voltage X-rays were as follows: 200–250 kV, 15 to 20 mA, H.V.L. 1·5 to 3·2 mm. Cu, F.S.D. 50 cm., in other words conventional X-rays. Undoubtedly this is still so in many centres.

Various techniques have been elaborated for this purpose. One commonly employed for treating the whole abdomen is a three-field arrangement. Two anterior fields, each 30 × 20 cm. are angled at 120 degrees to each other, and extend from the level of the twelfth dorsal vertebra to the groin: posteriorly there is one field 30 cm. in diameter. Alternatively four fields are sometimes preferred, two anterior and two posteriorly oblique each 30 × 20 cm. The beams are arranged to deliver a homogeneous irradiation to the whole potentially diseased volume.

To achieve this in practice—and it is the first essential of successful treatment—constant and accurate aiming of the beam throughout the course of treatment is necessary. It is ensured by beam directional devices such as the protractor, the pin and arc, or specially designed jigs such as the trunk bridge developed at the Christie Hospital, Manchester, by Tod (1944). With such instruments the irradiation beams can be directed precisely at the prescribed angle and at the exact entrance points. These techniques irradiate such a large volume of tissue that the dose rate must be carefully controlled. All the fields are treated daily, 50 r being delivered initially to each. The dose is increased by 10 r per day until a dose of 100 r per field per day is reached.

The response to irradiation varies greatly with the histological type of the tumour, the seminoma being in the majority of cases more radiosensitive than the teratoma. Complete and lasting regression of some metastatic tumours has been observed with doses as low as 2,000 r. Where possible a minimum tumour dose of 3,000 r in four to five weeks ought to be aimed at. However, both the total dose likely to be tolerated by any patient, and the rate at which it is delivered, are limited by the general reaction of the patient as well as by the local reaction of the normal tissues and organs surrounding the diseased area.

The general reaction is dependent upon the volume and site irradiated. Where the large field techniques described above are used this comprises nearly the whole abdomen as well as the bones of the lumbar vertebræ and the pelvis. Therefore, as might be expected, treatment is often attended by nausea and even vomiting, as

well as a severe fall in both the total white cell and lymphocyte counts. It is our experience that the general reaction associated with the use of these large field techniques is such as to limit the delivery of an adequate lethal tumour dose in a considerable proportion of cases, even to the relatively radiosensitive seminomas. Moreover, as pointed out by Paterson (1952) and by Kunkler *et al.* (1952), it is dangerous to irradiate the whole of both kidneys to a dose in excess of 2,000 r in five weeks or less. In our opinion the risk of so doing by the use of wide-field irradiation beams is considerable. Actually those cases in which these authors observed renal damage were in fact treated by fields even larger (40 to 45 cm. × 17 to 20 cm.) than those referred to in the techniques outlined above. For these reasons we recommend that the large-field techniques should be reserved for cases with metastases already widespread throughout the abdomen and that a technique using other rather smaller fields be adopted for all but these advanced cases (Prossor, 1951). The iliac and para-aortic nodes are treated in one stage using opposing 15 × 15 cm. fields to the iliac and lower para-aortic glands and 20 × 10 cm. to the upper para-aortic glands and the glands at the level of the renal vessels, delivering 2,500 r–3,500 r in thirty to thirty-five days. When the tumour has been found at operation to have transgressed the tunica albuginea the inguinal nodes are also treated.

The general reaction varies with the site and volume of the tissues irradiated as well as with the quality of the rays. In these cases the volume necessarily comprises a large proportion of the abdomen, irradiation of which hitherto usually tended to cause nausea and diarrhœa. The vertebræ are also included in the treatment volume and the effect on the marrow sometimes produced a severe fall in the white cell count. These general reactions, together with the local reaction of the normal tissues surrounding the nodes, intestinal canal and skin, limit the total quantity of irradiation which can be given as well as the rate at which it is administered.

The effect is such that, although an adequate dosage can be administered with conventional X-rays to destroy the radiosensitive seminoma, irradiation of this quality cannot deal adequately with the relatively insensitive teratomas, a fact well illustrated by the survival figures for the two diseases. No less than 75% of cases of seminoma presenting with no initial clinical evidence of metastases survived five years. This compares with a figure of 46% for a similar group of teratomata, similarly treated by simple orchidectomy and post-operative treatment with conventional X-rays. In an attempt to improve the control of this disease by super-voltage irradiation, as well as to assess the effect of X-rays generated at 2 MeV, all cases of teratomata of the testes seen at the Westminster Hospital since 1954 have been treated post-operatively on the Van de Graaf generator (all have had simple orchidectomy) and the abdominal lymph nodes have been irradiated through two elongated (sometimes L-shaped) fields. These are designed to cover the upper and lower para-aortic groups of nodes but avoid the kidney parenchyma. The iliac nodes on the homolateral side are included in an L-shaped extension from the main field. Constant and accurate beam direction is ensured by radiography using the therapeutic beam itself with special screens. In prophylactic cases the field size has varied from 31 × 13 cm. to 24 × 10 cm. The dose has been at the rate of 230 r daily, and 4,500 r to 5,000 r has been delivered in thirty days.

In no cases treated by this method has any untoward systemic reaction been observed. One only caused anxiety because of a sharp fall in the white blood count which recovered rapidly when the treatment was stopped and two had slight diarrhœa. Skin reactions are very mild—slight pigmentation and dry peeling at the worst and only mild erythema in the majority of cases. In no case has any severe desquamation been noted, nor has there been any intestinal injury or kidney damage.

Although it is only four years since the first patient in this series completed treatment, it is fair to say that the results are at least encouraging. 40 patients presented in the first instance without clinical evidence of metastases; 28 are alive and well with no evidence of disease.

7 patients came in the first instance with disease already clinically obvious in the para-aortic nodes or elsewhere. Only one of these is alive and free from disease, but in every one there occurred very satisfactory regression of the lymph node enlargement following treatment, and we are satisfied that the palliation was achieved with a minimum of discomfort to the patients.

To summarize, these cases demonstrate many of the outstanding clinical advantages of 2 MeV X-rays.

The increase in the percentage depth dose has allowed an adequate tumour dose to be delivered at nearly all depths by the simplest and most accurate techniques.

The decrease in dose received at the level of the skin compared with the subcutaneous tissues has resulted in minimal surface reactions.

Generally speaking patients have tolerated radical treatment better and it is possible to give

palliative treatment with less disturbance to the patient than with conventional X-rays.

The decrease in the amount of lateral scatter and the improvement in the sharpness of collimation of the beam allows a minimal dosage to structures outside it—for example, the kidneys—and the total body dose and integral dose is far less than that for similar field size with 250 kV.

Finally the abdomen and pelvis tolerate well doses of the order of 4,500 r to 5,500 r in six weeks and this appears adequate to produce very satisfactory and even lasting regression of abdominal metastases from teratomata of the testes.

Analysis of material.—The cases in our series have been divided into two groups: (1) Those who were treated by high voltage X-rays before there was any clinical evidence of metastases in the para-aortic nodes, lungs or elsewhere, i.e. prophylactic irradiation, and (2) Cases who came in the first instance with metastases in the para-aortic nodes, lungs or elsewhere.

The five- and ten-year survival rate has been estimated in both groups on the cases seen between 1936 and 1953.

In the first group 151 were seen before 1953 and are therefore available for analysis (Table I).

TABLE I.—NEOPLASMS OF THE TESTIS
5 Years Follow Up 1938–1953

Group 1.	Orchidectomy.	Prophylactic irradiation
151 cases	97 seminoma ..	73 alive (75·4%)
	54 teratoma ..	25 alive (46·3%)

In the second group, 41 cases were treated between 1936 and 1953. 15 were teratomata and 13 were seminomata and in 13 there was no histological proof.

8 are alive and free from disease five or more years after treatment. This represents a five-year symptom-free survival of 19% (Tables II and III).

TABLE II.—NEOPLASMS OF THE TESTIS
5 Years Follow Up 1936–1953

Group 2. Cases presenting with metastases.

41 cases	13 seminoma	8 alive (19·5%)
	15 teratoma	
	13 not proved histologically	

TABLE III.—TUMOURS OF THE TESTIS
Analysis of 192 Cases

Group	Histology		Survived at least 5 years
1. Clinically free from metastases when first seen	Seminoma	(97 cases)	73 (75·4%)
	Teratoma	(54 cases)	25 (46·3%)
2. Having metastases when first seen	Seminoma	(13 cases)	3
	Teratoma	(15 cases)	2
	Undetermined	(13 cases)	3
	Total	192 cases	106

The ten-year figures are very similar (Tables IV and V).

TABLE IV.—NEOPLASMS OF THE TESTIS
10 Years Follow Up 1938–1948

Group 1.	Orchidectomy.	Prophylactic irradiation
70 cases	51 seminoma ..	38 alive (74·5%)
	19 teratoma ..	9 alive (47%)

TABLE V.—NEOPLASMS OF THE TESTIS
10 Years Follow Up 1936–1948

Group 2. Cases presenting with metastases

33 cases	11 seminoma	5 alive (15%)
	9 teratoma	
	13 not proved histologically	

Prognosis.—It can be seen that both the stage of the disease and the histological type of the tumour have an important bearing upon the prognosis.

It is best in those patients with seminoma treated before there is clinical or other evidence of metastases. Thus 74% of such patients are alive and free from disease ten or more years after treatment.

It is less favourable in patients with teratomata, but 47% of patients without metastases when first treated are alive and well after ten years.

The prognosis is much more unfavourable in those patients who present in the first instance with metastases present, but even in this—the worst group—15% of the patients are free from disease ten years after treatment by irradiation.

Acknowledgment.—I wish to thank my colleagues at the Westminster Hospital for permission to include their patients.

REFERENCES

CADE, S. (1952) Malignant Disease and its Treatment by Radium. Bristol; Vol. 4.

GORDON-TAYLOR, G., and WYNDHAM, N. R. (1947) *Brit. J. Surg.*, **35**, 6.

HANDFIELD-JONES, R. M. (1924) *Lancet*, ii, 850.

HINMAN, F. (1933) *Surg. Gynec. Obstet.*, **56**, 450.

JAMIESON, J. K., and DOBSON, J. F. (1910) *Lancet*, i, 493.

KUNKLER, P. B., FARR, R. F., and LUXTON, R. W. (1952) *Brit. J. Radiol.*, **25** 190.

LEWIS, L. G. (1949) In: Advances in Surgery. Edited by W. D. Andrus *et al.* London and New York; Vol. 2.

PATERSON, R. (1952) *J. Fac. Radiol., Lond.*, **3**, 270.

PROSSOR, T. M. (1951) *Brit. J. Surg.*, **38**, 473.

SAUER, H. R., WATSON, E. M., and BURKE, E. M. (1948) *Surg. Gynec. Obstet.*, **86**, 591.

SNELLING, M. D., and CONES, D. M. T. (1950) *Postgrad. med. J.*, **28**, 145.

TOD, M. C. (1944) *Proc. R. Soc. Med.*, **37**, 722.

A Technical Advance in Irradiation Technique

By Anthony Green, F.R.C.S., F.F.R.

London

This paper concerns a possible advance in the evolution of accuracy in radiotherapy, which has been one of my main interests for many years past. For convenience, this evolution is divided into four stages.

Stage I.—*Beam directioning.*—Giving accuracy at a point by using the back pointer.

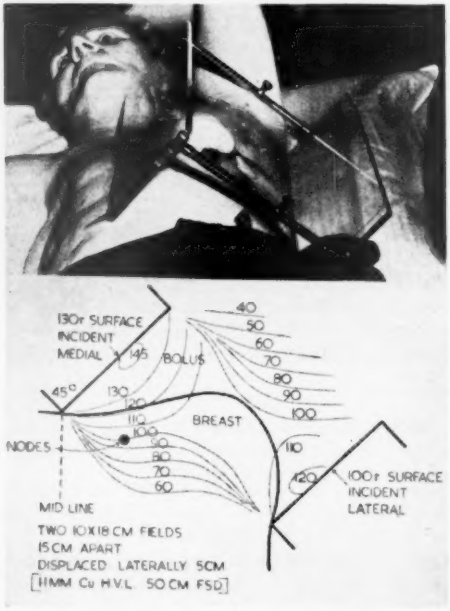


Fig. 1.—Uniform surface dose.

Stage II.—*The use of jigs.*—Fig. 1 shows a new jig to treat the internal mammary nodes and the breast with a uniform dose.

Stage III.—A *deeply* placed uniform zone is obtained by *moving beam treatment.* It is very gratifying to see this in use for many new cobalt units.

Stage IV.—*Tracking the disease.*—To date we have, in the main, applied uniform dose zones in the form of modified spheres, cylinders and so on to the treatment of disease, but the spread of disease cannot be expressed in terms of geometric shapes.

Spread of disease in carcinoma of the cervix.—Metal clips have been applied at the Royal Northern Hospital by Dr. M. Peters along the site of nodes commonly involved by this disease. For this a track has been drawn which shows the lymph-node spread. Fig. 2 shows a track obtained from X-ray pictures of the clips.

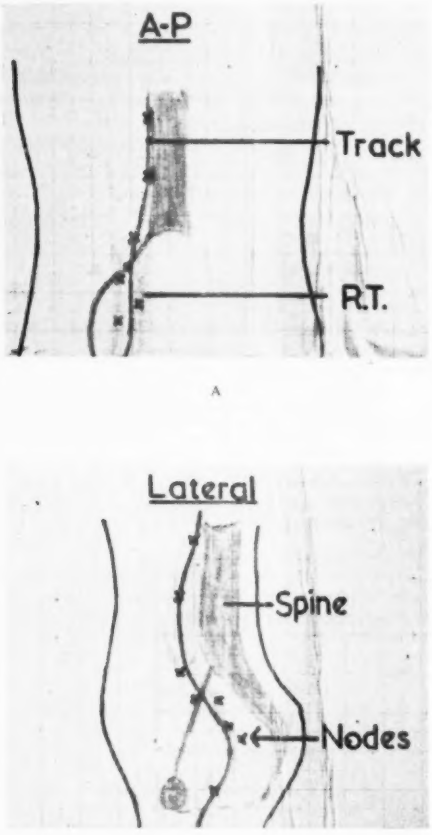


Fig. 2.—A possible method for carcinoma of the cervix.

Surely, it is more intelligent to make our radiation follow the track than heavily dose a large volume of tissue all around it.

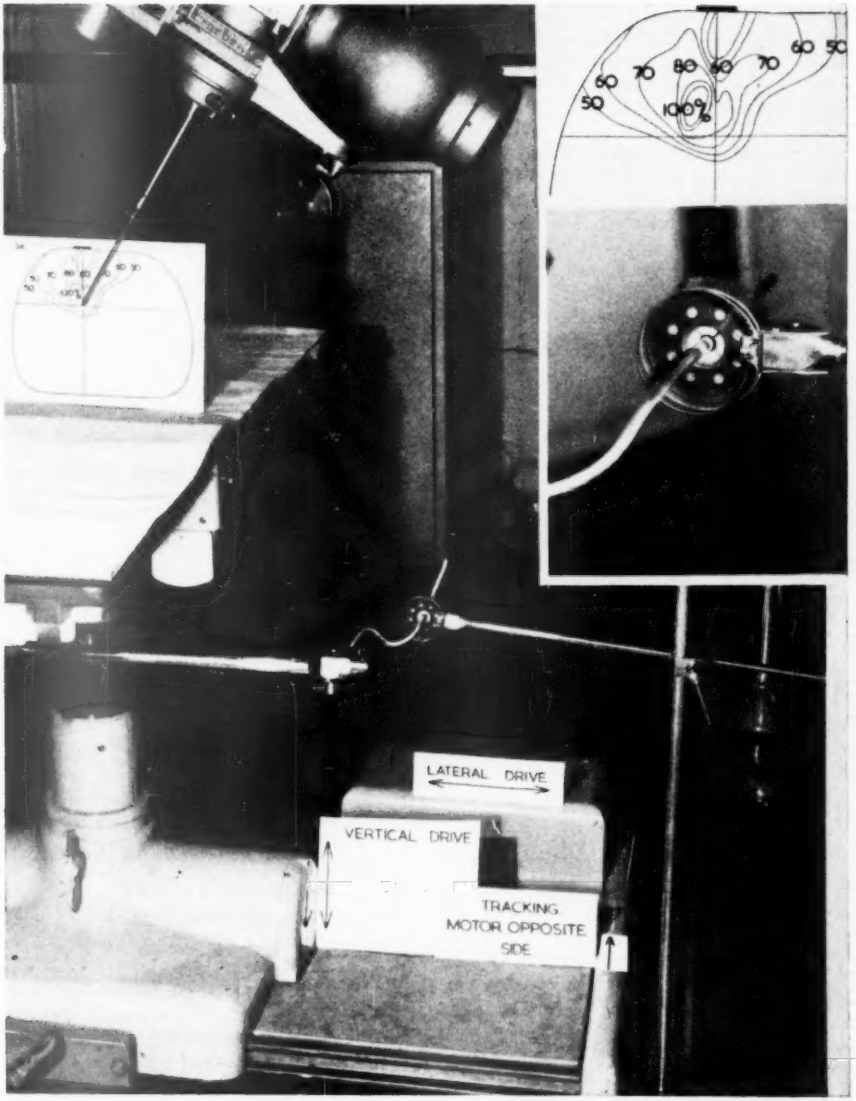


FIG. 4.—Method of tracking by arc moving beam therapy developed at the Royal Northern Hospital, London.

This has two advantages: (1) It spares the total volume of tissue raised to high dose, thus reducing the possible radiation damage, both early and late, to the structures in that volume. (2) Being a more limited volume, it may possibly be raised to a higher dose with more chance of eliminating the disease.

This principle of accurately following the pathological and anatomical spread of disease is earnestly commended. It may make some of us more conscious of our present shortcomings and possibly point the way to progress.

We should not be balked by the difficulties, even though they may be troublesome and many,

but should strive hard towards a better horizon. We are now armed with machinery giving millions of volts and powerful radioactive units. Let us use them with a high standard of skill, so that only the disease volume and not large tracts of tissue are intensively irradiated.

An electro-mechanical method of tracking.—In the case of a patient with a malignant testicular tumour the method for irradiation of the external iliac nodes, next the common iliac nodes and finally the para-aortic nodes is as follows: A rod is bent to the track in order to radiate the nodes (Fig. 3).

FIG. 3.—Track for malignant testicular tumour.

The method of obtaining this particular track was guided from an aortogram, pathological and anatomical studies. Next the shape and size of the volume of tissue around the track is chosen at will. From this is calculated the size of field and mode of application in order to obtain it. Commencing at the external iliac region, the radiation beam is made to follow the track by propelling the treatment table towards the para-aortic nodes. The beam is maintained accurately by a ring of electrical contacts surrounding the track guide (Fig. 4).

I have to thank our research technician at the Royal Northern Hospital, Mr. H. M. Christie, and Dr. W. A. Jennings of the Physics Department, who helped guide his work for distribution of dose at 250 kV.

By the courtesy of Professor B. W. Windeyer, Director of Radiotherapy at the Mount Vernon Hospital, the Physics Department there under Mr. D. E. A. Jones, after discussion with me, provided these distributions of dosage for ^{60}Co and 4 MeV for the para-aortic region only (Fig. 5).

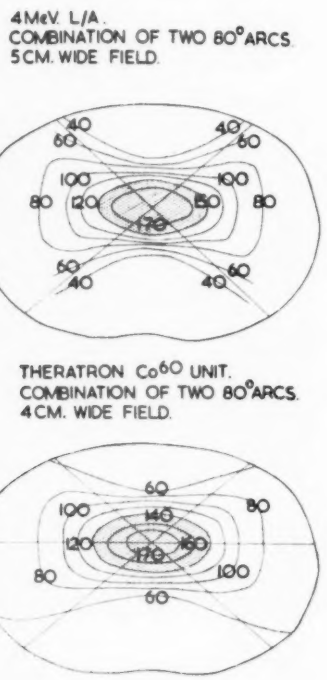


FIG. 5.

I might add that the master guide can be adapted to any prescribed track in the body and is useful, e.g. in the oesophagus.

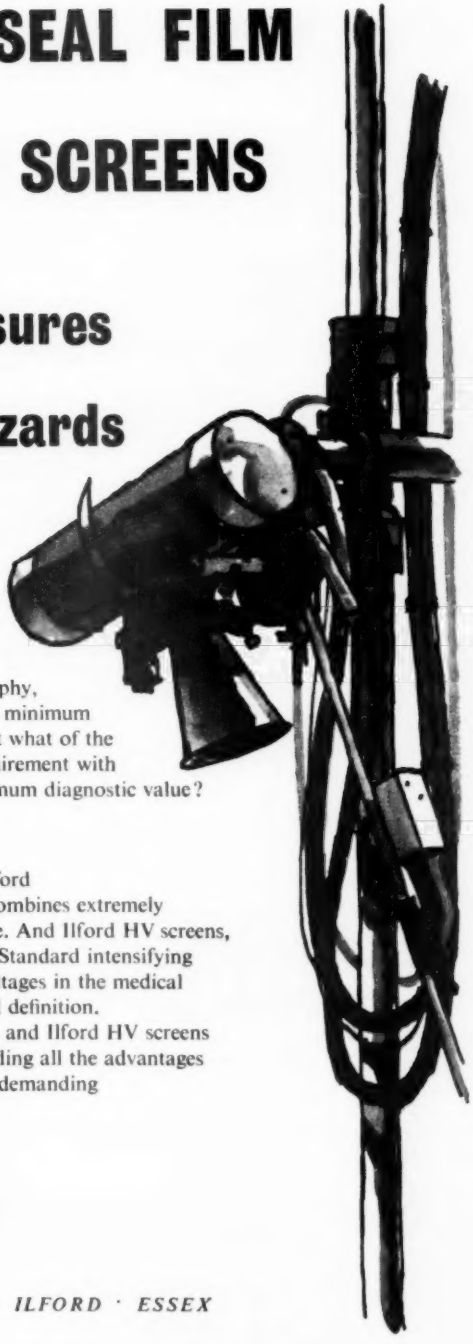
This is my contribution to the problem, but please regard it as only a primitive attempt from which I hope you yourselves will be able to advance.

ILFORD RED SEAL FILM

+ ILFORD HV SCREENS

= reduced exposures

= diminished hazards



Throughout the field of medical radiography, the desirability of keeping exposures at a minimum is a theme that needs no elaboration. But what of the practical problem of reconciling this requirement with the ever-present need for results of maximum diagnostic value?

TEAMWORK IS THE SOLUTION

Ilford Red Seal film is twice as fast as Ilford Standard X-ray film, yet it successfully combines extremely high speed with outstanding performance. And Ilford HV screens, although considerably faster than Ilford Standard intensifying screens (particularly at the higher kilovoltages in the medical range), are designed to give equally good definition. The combination of Ilford Red Seal film and Ilford HV screens thus forms a powerful partnership, affording all the advantages of exceptionally high sensitivity without demanding any sacrifice of radiographic quality.

ILFORD

ILFORD LIMITED · ILFORD · ESSEX

In peptic ulcer the mainstay of

treatment is the continuous control of acidity.

Nacton is a British drug which specifically

inhibits gastric secretion of acid and

REDUCES ACIDITY BY 50–70%

Nacton is long acting; doses given three times a day

and at bedtime give continuous relief

DAY AND NIGHT

At dose levels giving full control

of gastric secretion Nacton is

WITHOUT SIDE-EFFECTS

and has no anti-cholinergic activity other

than the inhibition of gastric secretion of acid

Nacton IN PEPTIC ULCER

Packages of 50 and 250 tablets

Each tablet contains 2 mg. of (1-methyl-2-pyrrolidyl)

methyl benzilate methyl methosulphate

a product of the

BEECHAM RESEARCH LABORATORIES

for

C. L. BENCARD LTD. Park Royal, London, N.W.10

Section of Experimental Medicine and Therapeutics

President—M. L. ROSENHEIM, C.B.E., F.R.C.P.

Meeting
December 9, 1958

SYMPOSIUM ON SOME NEW APPROACHES TO CALCIUM METABOLISM

Dr. G. Alan Rose[1] (London):

The Relative Importance of the Ionized and Complexed Fractions of Calcium in Human Plasma in Control of the Urine Calcium

There is frequently a remarkable lack o correlation between the plasma calcium and the urine calcium, even in the presence of what appears to be normal renal function. Thus a patient with parathyroid adenoma and elevated plasma calcium had a low urine calcium attributed to accompanying steatorrhœa (Davies *et al.*, 1956). Conversely normal plasma calcium is frequently present in idiopathic hypercalciuria. The normal urine calcium of approximately 120–250 mg. a day is only a very small fraction of the total plasma calcium of about 86 grams which passes through the kidneys with the blood each day. If we assume, although there is no evidence for this, that the plasma protein-bound calcium does not pass into the glomerular ultrafiltrate in significant amount, then the total calcium available for excretion is reduced to about 10·5 grams a day. This figure is still far above the observed daily urine calcium so that nearly all of the ultrafiltered calcium must be reabsorbed. Nearly all of the *in vitro* ultrafiltrable calcium is ionized, although a small fraction is diffusible but not ionized and includes about 0·2 mg./100 ml. of calcium complexed to citrate (Rose, 1957). If this citrate-bound fraction alone were excreted in the urine then the daily urine calcium would be about 350 mg. This figure is so close to the observed values that we have considered it worth while to devise experiments intended to assess the importance of plasma complexed calcium in control of urine calcium, as compared with the ionized calcium. Data available from the literature on this point are scanty. Chen and Neuman (1955) following experiments on dogs suggested that urine calcium might be dependent upon a non-ionized but ultrafiltrable complex of calcium, while the data of Freeman and Chang (1950) suggest that in dogs the plasma citrate-bound calcium may be considerably more important than the plasma ionized calcium in controlling urine calcium. Data from human subjects are even more scanty.

Our experimental approach has been to infuse intravenously in approximately two minutes into normal volunteers either calcium chloride, to raise the plasma ionized calcium by about 1·5 mg./100 ml., or sodium citrate, to raise the plasma complexed calcium by about the same amount. The exact effects of these infusions upon the plasma calcium fractions, and upon the plasma citrate, and urinary calcium and citrate have been observed and compared. The results are presented in shortened form: the detailed results are to be published elsewhere (Harper *et al.*, 1959).

Fig. 1 illustrates the results of the calcium

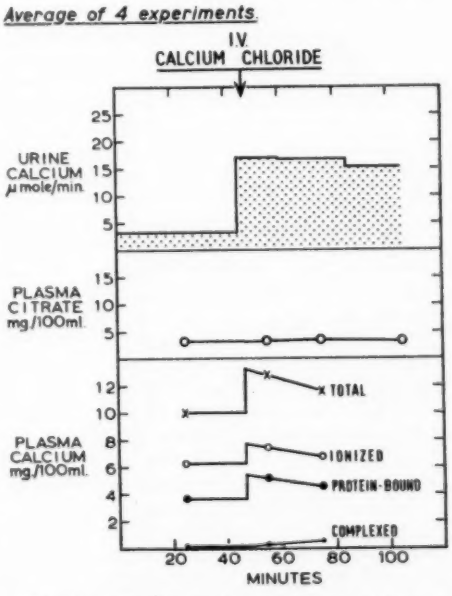


FIG. 1.—Effect of rapid intravenous infusion of calcium chloride on urine calcium, plasma citrate and calcium fractions of normal human subjects.

[1]In receipt of a grant from the Medical Research Council.

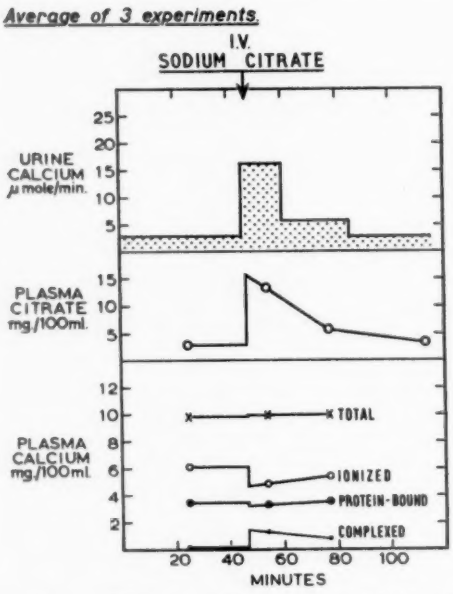


FIG. 2.—Effect of rapid intravenous infusion of sodium citrate on urine calcium, plasma citrate and calcium fractions of normal human subjects.

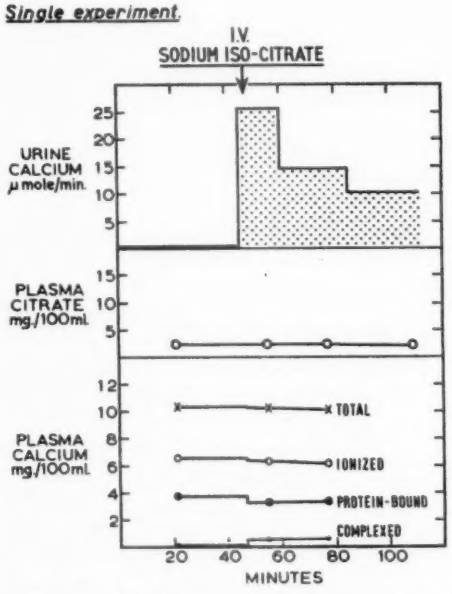


FIG. 3.—Effect of rapid intravenous infusion of sodium isocitrate on urine calcium, plasma citrate and calcium fractions of a normal human subject.

chloride infusions. The rise in plasma ionized calcium was followed by an immediate and approximately sixfold rise in the urine calcium. Such results are similar to those of the many others who have infused calcium gluconate, although comparison is difficult in view of the differing time scales. Fig. 2 shows the results of the sodium citrate infusions. Despite a fall in the plasma ionized calcium which might have been expected to result in a fall in urine calcium, an immediate sixfold increase in urinary calcium was observed. It is deduced that this calcium diuresis was due to elevation of the plasma complexed calcium. The calcium diuresis of citrate infusion was poorly sustained because of the rapid rate of fall of plasma citrate after the infusion, this presumably being due mainly to metabolism of citrate rather than to urinary excretion.

Sodium isocitrate was also infused into one individual in order to see whether citrate was specific in its ability to induce calcium diuresis. The results (Fig. 3) showed that a comparable dose of isocitrate caused a smaller rise in plasma complexed calcium than did the citrate (since the formation constant of calcium isocitrate is less than that of calcium citrate) but that this rise was apparently better sustained than the rise after citrate infusion. Following this infusion the rise in urine calcium was the largest which we observed in our series, and it was better sustained than the calcium diuresis which followed citrate infusion. We have therefore deduced that the calcium isocitrate complex had a higher renal clearance than the calcium citrate complex, and indeed it appears likely that the calcium isocitrate complex was being excreted at the rate of glomerular ultrafiltration.

Calcium gluconate infusions lead to sodium diuresis (Freedman *et al.*, 1958), so that it was thought necessary to give a control sodium chloride infusion and observe the effect of this upon urine calcium. No significant rise in urine calcium was observed. Following citrate infusion, the urine was tested for reducing substances, and for amino acids by paper chromatography, and no increases were noted.

The clinical implications of these observations are considerable. It is clear from our results that a large rise in urine calcium may be due to a small rise in either the ionized or complexed fractions of calcium in the plasma. Although the point is not completely proven it seems likely from our data that under normal conditions these fractions contribute to the urine calcium in approximately equal proportions. In any case, however, it may be inferred that a rise of 50% in urine calcium may be due to a rise in plasma

complexed calcium of only 0·3 mg./100 ml. Such a rise would hardly be considered significant if only the total plasma calcium were to be measured, and the latter value would indeed probably be within normal limits. Perhaps it is hardly surprising therefore that there is sometimes little correlation between plasma calcium (total) and urine calcium. In vitamin-D therapy the urine calcium may rise before there is any change in plasma (total) calcium. This is now readily explained when it is recalled that vitamin D raises the plasma citrate (Harrison and Harrison, 1952). It is possible that some cases of "idiopathic" hypercalciuria might be due to disturbance of citrate metabolism and that this substance might then be raised in the plasma leading to "overflow" of calcium citrate complex into the urine. Alternatively, there might be a failure of the renal tubules to reabsorb the calcium citrate complex other things being normal. Other cases, however, of "idiopathic" hypercalciuria might be due to similar disturbances in metabolism of isocitrate. We would suggest that other organic acids known to occur in plasma should also be tested to see if they can induce calcium diuresis, and that examination of plasma organic acids provides another test which should be carried out before a hypercalciuria can truly be labelled "idiopathic".

REFERENCES

CHEN, P. S., and NEUMAN, W. F. (1955) *Amer. J. Physiol.*, **180**, 623.
DAVIES, D. R., DENT, C. E., and WILLCOX, A. (1956) *Brit. med. J.*, ii, 1133.
FREEDMAN, P., MOULTON, R., and SPENCER, A. G. (1958) *Clin. Sci.*, **17**, 247.
FREEMAN, S., and CHANG, T. S. (1950) *Amer. J. Physiol.*, **160**, 335.
HARPER, C., LLOYD, H. M., ROSE, G. A., and WATSON, L. (1959) In preparation.
HARRISON, H. E., and HARRISON, H. C. (1952) *Yale J. Biol. Med.*, **24**, 273.
ROSE, G. A. (1957) *Clin. Chim. Acta*, **2**, 227.

Dr. Lyal Watson[1] (London):

Citrate Metabolism in Hyperparathyroidism

Since Dickens (1941) demonstrated that bone mineral is rich in citrate, which comprises about 1% of normal bone, there has been increasing interest in the role of citrate in bone physiology and in the interrelationships of calcium and citrate metabolism generally. Dixon and Perkins (1952) showed the presence in bone of citrogenase and aconitase, enzymes necessary for citrate synthesis, and suggested that the citrate found in bone mineral might be produced locally by bone cells. Neuman and Neuman (1958) elaborated this point and proceeded further to speculate that much of the plasma citrate might also be derived from bone and to develop an interesting concept of skeletal dynamics which attributes vital roles to citric acid and the parathyroids.

These workers have shown that the circulating fluids are normally supersaturated with calcium and phosphorus in relation to the bone mineral, so that the purely physico-chemical tendency is for mineral deposition. Since bones do not progressively fossilize, there must be an active physiological mechanism to ensure bone mineral dissolution and to maintain the dynamic equilibrium of bone deposition and resorption.

Citric acid may play a vital role in this process. It is an admirable substance for the purpose, for, among other desirable properties, it forms with calcium a chelate, a highly associated compound in which calcium is soluble but unionized and may therefore be transported from bone to blood stream against an ionic gradient. This calcium can then be made available in the ionized form by the simple device of utilizing the citrate in the tissues.

Neuman and Neuman consider that the whole process is regulated by the secretions of the parathyroid glands. Neuman *et al.* (1956) performed an experiment in which they were able to sample blood directly from the spongiosal circulation of the femur of an intact dog and to demonstrate a dramatic increase in citrate output from the bone almost immediately after the injection of a parathyroid extract. They summarized their conclusions as follows: "A parathyroid-controlled citrate gradient maintains a steady but supersaturated level of ionized calcium in serum".

Much other evidence is available to indicate a parathyroid influence on citrate metabolism. Harrison (1956) reported low plasma citrate levels in hypoparathyroidism, and Shorr *et al.* (1942) an increase in urinary citrate following the administration of parathyroid hormone to a hypoparathyroid subject. Dickens (1941) produced an increase of 27% in bone citrate by prolonged administration of parathyroid hormone to a pup. Alwall (1944), L'Heureux and Roth (1953), and Elliott and Freeman (1956*b*) all showed that the administration of parathyroid extracts would raise the plasma citrate level in experimental animals. Elliott and Freeman (1956*a*) also demonstrated that the transient elevation of plasma citrate which follows

[1]Travelling Scholar in Medicine of the Royal Australasian College of Physicians for 1957, and in receipt of a grant from the Adolph Basser Research Funds of the College. Present address: Sydney Hospital, Macquarie Street, Sydney Australia.

nephrectomy in certain species depends upon the integrity of the thyroid-parathyroid apparatus. The plasma citrate level did not rise following nephrectomy in parathyroidectomized rats but the response was restored to the preparation by the administration of parathyroid extracts. Finally, high blood citrate levels were found in hyperparathyroidism with bone disease by Sjöström (1937), Herbert (1949) and Harrison (1954). These authors did not comment on the plasma citrate findings in hyperparathyroidism without bone disease. Shorr *et al.* (1948) also reported high plasma citrate levels in cases of hyperparathyroidism without specifically stating which type of disease they were investigating.

Material, Methods and Results

Plasma citrate levels were determined in 12 patients with hyperparathyroidism proven by the removal of a parathyroid adenoma at operation. The blood urea and the serum alkaline phosphatase were normal in all cases, nor was there any radiological evidence of hyperparathyroid bone disease. Unfortunately no suitable case of hyperparathyroidism with bone disease was available during this study.

All the blood samples were collected from patients in the fasting state. The plasma citrate was determined by the method of Ettinger *et al.* (1952). Twenty-eight determinations on 19 normal individuals gave a range of 2·1–3·6 mg./100 ml. by this method.

The pre-operative plasma citrate levels in the 12 patients with hyperparathyroidism without bone disease are shown in the left-hand column of Fig. 1. The values were within the normal range in 9 of the 12 cases and in only 1 case was there any pronounced elevation of the plasma citrate. Although there appeared to be a slight rise of the plasma citrate levels in comparison with normals, the mean of the group was 3·2 mg./100 ml. compared with a mean of 2·8 mg./100 ml. in the control group, a difference not statistically significant.

Discussion.—This finding of a normal plasma citrate level in most cases of hyperparathyroidism without bone disease is in contrast with the reported findings in cases of hyperparathyroid bone disease and after administration of parathyroid extracts in experimental animals. The most likely reason for this is that we are dealing with different case material. Other differences between cases of hyperparathyroidism with and without bone disease are well recognized and these data appear to establish another point of difference.

It is of interest to consider the occurrence of normal plasma citrate levels in hyperparathyroidism in connexion with the concept of a parathyroid controlled release of citrate from bones. Blood levels alone do not disprove an osseous action since citrate occupies a central position in metabolism so that great changes in citrate turnover could occur without significant alteration in blood levels, if increased production were balanced by increased utilization.

There is increasing acceptance of the idea of a dual action of parathyroid secretions (Dent, 1953) and some speculation that the glands may actually produce different hormones with different actions (Davies and Gordon, 1953*a*, *b*). If this is true, it could well explain the differences between cases of hyperparathyroidism with and without bone disease and these data provide another piece of evidence which may favour such a theory. It is easy to imagine different parathyroid adenomas producing different hormonal secretions and the patients under consideration may have been producing little, if any, excess of the bone-regulating hormone.

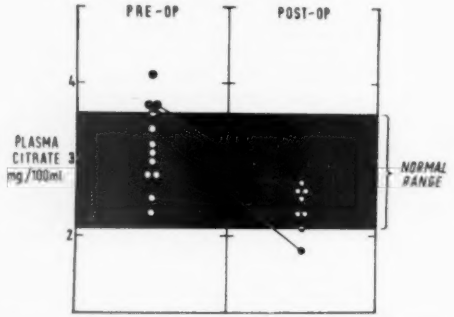


FIG. 1.—Plasma citrate levels (fasting) in hyperparathyroidism without bone disease.

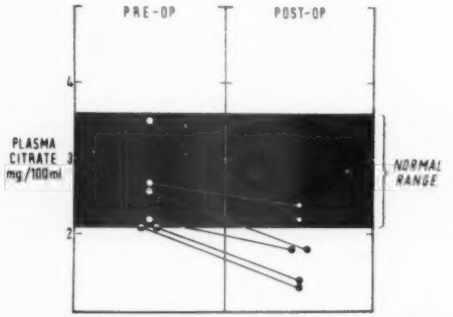


FIG. 2.—Plasma citrate levels (fasting) in operations of election.

Post-operative Studies

The study of post-operative plasma citrate levels in these patients brought to light another interesting facet of citrate metabolism. In 8 of the 12 patients the plasma citrate was determined about one week after removal of the adenoma. These values are shown in the right-hand column of Fig. 1. In every case the plasma citrate level fell after operation. This might have been explicable as post-operative hypoparathyroidism.

As controls, 6 other patients were selected having routine operations of election. Blood was taken immediately before operation and seven days post-operatively in each case, and the plasma citrate levels (Fig. 2) showed the same response as in the parathyroid group.

Discussion.—It appears that low plasma citrate levels post-operatively are a non-specific response to the trauma and stress of operation and anæsthesia. Metabolic responses to surgery are, of course, well known but little attention has been paid to these changes in plasma citrate in articles published in the English language. Nevertheless post-operative low plasma citrate levels were described by the Scandinavians many years ago. Working in a surgical clinic, Sjöström (1937) found them after operations of many different kinds.

This response may be due to the outpouring of adrenal corticoids known to occur after surgery. It was shown by Pincus *et al.* (1951) in the rabbit, by Harrison *et al.* (1958) in the rat and by Henneman and Henneman (1958) in man that increased serum concentrations of 17-hydroxy-corticoids produced a marked fall in plasma citrate levels. Henneman and Henneman also observed a low urinary citrate in four patients after either laparotomy or open reduction of fractures and thought that the response in these cases was due to a stress reaction with adrenal cortical overactivity. It seems probable that the low plasma citrate levels seen in all these patients were due to the same mechanism.

Summary and Conclusions

(1) Most patients with hyperparathyroidism without bone disease have normal plasma citrate levels. This is quite different from the high plasma citrate levels reported in cases of hyperparathyroidism with bone disease and appears to provide another point of difference between the two clinical groups. A possible explanation of these differences has been advanced.

(2) Low plasma citrate levels occur non-specifically after many surgical operations, and may be due to the excessive production of adrenal cortical steroids which is known to occur in response to surgery.

Acknowledgments.—The author wishes to express his thanks to Professor C. E. Dent for permission to publish the case material, to Professors M. L. Rosenheim and C. E. Dent for providing facilities for the investigation in the Medical Unit, University College Hospital, London, and to the Royal Australasian College of Physicians for its support.

REFERENCES

ALWALL, N. (1944) *Acta med. scand.*, **116,** 337.
DAVIES, B. M. A., and GORDON, A. H. (1953*a*) *Nature, Lond.*, **171,** 1122.
——, —— (1953*b*) *J. Endocrin.*, **9,** 292.
DENT, C. E. (1953) *Proc. R. Soc. Med.*, **46,** 291.
DICKENS, F. (1941) *Biochem. J.*, **35,** 1011.
DIXON, T. F., and PERKINS, H. R. (1952) *Biochem. J.*, **52,** 260.
ELLIOTT, J. R., and FREEMAN, S. (1956*a*) *Endocrinology*, **59,** 181.
——, —— (1956*b*) *Endocrinology*, **59,** 196.
ETTINGER, R. H., GOLDBAUM, L. R., and SMITH, L. H., Jr. (1952) *J. biol. Chem.*, **199,** 531.
HARRISON, H. C., HARRISON, H. E., and PARK, E. A. (1958) *Amer. J. Physiol.*, **192,** 432.
HARRISON, H. E. (1954) *Pediatrics, Springfield*, **14,** 285.
—— (1956) *Amer. J. Med.*, **20,** 1.
HENNEMAN, D. H., and HENNEMAN, P. H. (1958) *J. clin. Endocrin.*, **18,** 1093.
HERBERT, F. K. (1949) *Int. Congr. Biochem.*, 166.
L'HEUREUX, M. V., and ROTH, G. J. (1953) *Proc. Soc. exp. Biol., N.Y.*, **84,** 7.
NEUMAN, W. F., FIRSCHEIN, H., CHEN, P. S., MULRYAN, B. J., and DISTEFANO, V. (1956) *J. Amer. chem. Soc.*, **78,** 3863.
——, and NEUMAN, M. W. (1958) The Chemical Dynamics of Bone Mineral. Chicago.
PINCUS, J. B., NATELSON, S., and LUGOVOY, J. K. (1951) *Proc. Soc. exp. Biol., N.Y.*, **78,** 24.
SHORR, E., ALMY, T. P., SLOAN, M. H., TAUSSKY, H., and TOSCANI, V. (1942) *Science*, **96,** 587.
——, CARTER, A. C., SMITH, R. W., and TAUSSKY, H. (1948) Josiah Macy Jr. Conference on Metabolic Aspects of Convalescence. New York; **17,** 106.
SJÖSTRÖM, P. (1937) *Acta chir. scand.*, **79,** Suppl. 49.

Dr. B. E. C. Nordin (Glasgow):

Investigation of Bone Metabolism with ^{47}Ca—a Preliminary Report

There are certain aspects of mineral metabolism in relation to bone which cannot be investigated by conventional techniques. This applies in particular to the study of the absolute rates of new bone formation and bone destruction, as opposed to the net difference between formation

and destruction which can be determined by a balance. It is believed that a certain amount of new bone is formed every day and that in normal subjects an equivalent amount is destroyed, but the actual magnitude can only be measured by the use of a labelled substance which enables one to distinguish between the calcium which is going into, and that which is coming out of, the skeleton. A knowledge of the rate of these processes would be of great value in the elucidation of pathological processes, and is especially relevant to the pathogenesis of osteoporosis which is widely believed to be due to a reduction in the rate of formation of new bone, the process of resorption going on at the normal rate. While it is true that osteoporosis must be due to an imbalance between the rates of accretion (i.e. new bone formation) and resorption (i.e. bone destruction) there is no conclusive evidence as to which of these processes is disturbed in osteoporosis; but it is quite possible that the conventional explanation is incorrect and that the condition is due to increased resorption rather than reduced accretion.

Until quite recently, the only radioactive isotope of calcium available was ^{45}Ca, a beta-emitter with a long half-life which is unsuitable for use in human subjects, although it has been extensively used in human studies in the U.S.A. (Bronner *et al.*, 1956) and Sweden (Bauer *et al.*, 1955). However, the Atomic Energy Research Establishment at Harwell have now consented to manufacture small amounts of ^{47}Ca, an isotope with properties which make it very suitable for metabolic studies in humans, as can be seen in Table I. Owing to its relatively high cost,

TABLE I.—RADIATIONS FROM ^{45}Ca AND ^{47}Ca

	^{45}Ca	^{47}Ca
β:	0·26 MeV	0·7 and 2·0 MeV
γ:	None	0·5, 0·8 and 1·3 MeV
Half-life:	160 days	4·8 days
Decays to:	^{45}Ca (stable)	^{47}Sc (radioactive)
		Contamination with ^{45}Ca: 5%

irregular manufacture and short half-life the number of subjects we have studied with the isotope so far is very small, but the methods used and the results obtained may none the less be of interest.

The method of measuring bone accretion with isotopic calcium was devised by Bauer *et al.* (1955) and has been modified by Fraser (1957) in a strontium test. It depends upon the assumption that an injected isotope of calcium mixes with a definite quantity of exchangeable calcium in the tissue fluids and on the surface of the skeleton, and that the loss of activity from this exchangeable pool only takes place into the fæces, the urine and into new bone as it is formed (Fig. 1). Since the total loss of activity into the fæces and urine can be measured, and the total loss from

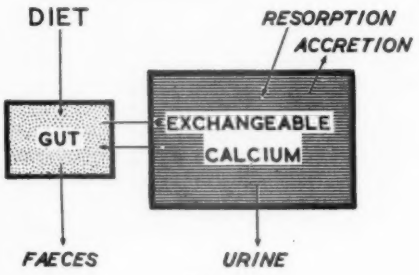


FIG. 1.

the pool can be calculated from the loss of specific activity in the body fluids, it is possible to calculate the amount of activity, and therefore the amount of calcium, going into the skeleton each day.

The subjects are given an intravenous injection of 10 microcuries of ^{47}Ca and the urine is collected in twenty-four-hour aliquots for seven days. The fæces are also collected daily for seven days starting one day after the injection. The total activity of urine and fæces is measured each day, as well as the amount of stable calcium excreted in the urine. The specific activity of the urine (percentage of dose per mg. calcium) is assumed to be the same as that of the extracellular fluid, and it is plotted on semilogarithmic paper against time as shown in Fig. 2. The line of best fit is calculated for these 7 observations and is extrapolated back to zero time, at which point the specific activity represents that which would have been observed had there been instant mixing. The percentage of the dose per mg. of calcium at zero time is then converted into the "exchangeable calcium" by dividing it into 100. From

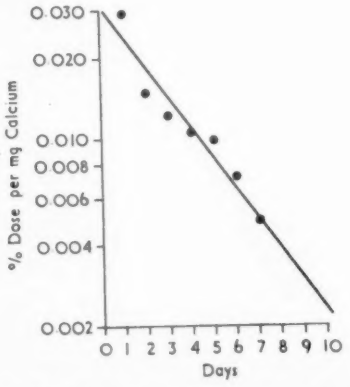


FIG. 2—Fall of specific activity in urine during first week after injection of ^{47}Ca in Case J. S.

the fall in specific activity, a constant fraction of which is lost each day, one can calculate the absolute amount of labelled calcium leaving the exchangeable pool. The average amount of calcium lost each day in the urine is then deducted from this figure, as is the amount calculated to have been lost in the fæces. (In calculating the endogenous fæcal calcium, the fæcal activity is converted into mg. of calcium on the basis of the specific activity of the urine of the previous day to allow for the time taken for matter to pass through the gut.) The total urinary and endogenous fæcal loss is then deducted from the total loss from the exchangeable pool to give the amount of calcium that has gone into bone by accretion. The procedure rests upon a number of assumptions of varying validity which it is not possible to discuss in this context. We are not entirely convinced that accretion is the only process measured by this calculation but it is the nearest approach to accretion which it is possible to measure at the present time.

Results

The results obtained in 7 normal subjects are shown in Table II. It will be seen that the exchangeable calcium ranges from 39 to 116 mg. of calcium per kg. body weight, and that the accretion rate ranges from 5·2 to 14·5 mg. of calcium per day per kg. body weight. The mean accretion rate in this group is 8·9 mg. calcium per kg. per day.

TABLE II.—NORMAL SUBJECTS

			Exchangeable calcium		*Endogenous fæcal calcium*	*Accretion rate*	
Sex	*Age*	*Weight (kg.)*	*(mg.)*	*(mg./kg.)*	*(mg./day)*	*(mg./day)*	*(mg./kg./day*
F	70	65	5,430	84	140	390	6·1
F	56	72	2,830	39	140	430	6·0
M	57	71	6,410	91	150	370	5·2
M	28	65	7,540	116	290	870	14·5
F	59	49	4,500	92	180	560	11·6
M	56	72	2,920	41	140	550	7·6
M	67	64	2,980	47	170	700	10·9

The results obtained in 7 patients with primary osteoporosis (i.e. of the type commonly called post-menopausal or senile) are shown in Table III. The exchangeable calcium ranges from 46 to 107 mg. Ca per kg. body weight, and the accretion rate from 7·6 to 17·7 mg. Ca per kg. body weight per day. The mean accretion rate in this group is 12·1 mg. Ca per kg. per day.

TABLE III.—OSTEOPOROSIS

			Exchangeable calcium		*Endogenous fæcal calcium*	*Accretion rate*	
Sex	*Age*	*Weight (kg.)*	*(mg.)*	*(mg./kg.)*	*(mg./day)*	*(mg./day)*	*(mg./kg./day*
F	64	60	3,290	54	80	650	10·9
F	67	50	3,890	78	220	520	8·5
F	70	34	2,800	83	80	610	17·7
F	67	34	3,640	107	90	600	16·3
F	62	45	2,920	65	170	680	15·0
F	64	54	2,460	46	70	410	7·6
F	72	74	3,960	53	120	810	11·2

It is evident that there is considerable variation within the two groups of 7 subjects, but there is certainly no suggestion whatever of a reduced rate of new bone formation in the patients with osteoporosis: if anything, it appears rather that their rate of bone formation is increased. Whedon and his colleagues (Heaney and Whedon, 1958) have recently reported results obtained with ^{45}Ca in 4 patients with osteoporosis and have also found that the accretion fell within their normal range. Thus these results, and those of Whedon, do not support the concept that osteoporosis is due to a reduction in the rate of new bone formation, but are rather compatible with the idea that the loss of bone in this condition is due to increased resorption. This is not the place to discuss the possible cause of this increased resorption, except to repeat what I have suggested elsewhere—that osteoporosis is perhaps the result rather than the cause of negative calcium balance (Nordin, 1958*a*). Such negative calcium balance could be due to inadequate intake, malabsorption or excessive urinary or fæcal excretion of calcium. Data in support of this view are being reported elsewhere (Nordin, 1958*b*).

REFERENCES

BAUER, G., CARLSSON, A., and LINDQUIST, B. (1955) *K. fysiogr. Sällsk. Lund Förh.*, No. 1, 25.

BRONNER, F., HARRIS, R. S., MALETSKAS, C. J., and CLEMENS, E. B. (1956) *J. clin. Invest.*, **35,** 78.

FRASER, R. (1957) *Proc. R. Soc. Med.*, **50,** 21.

HEANEY, R. P., and WHEDON, D. (1958) *J. clin. Endocrin.*, **18,** 1246.

NORDIN, B. E. C. (1958*a*) *Brit. med. J.*, i, 1415.

—— (1958*b*) Proceedings of the New Lankenau Conference on Bone as a Tissue. Philadelphia.

BOOKS RECENTLY PRESENTED AND PLACED IN THE SOCIETY'S LIBRARY

Académie de la République Populaire Roumaine. Congrés National des Sciences Médicales. Communications des invités étrangers, Bucarest, 5–11 Mai, 1957. pp. 908. Bucarest: A.R.P.R. 1959.

Berengo (A.). Etiologia e sistematica delle epatiti da virus. pp. 234. Pisa: Omnia Medica. 1957. (Two copies).

Brock (Sir Russell C.). The present position of cardiac surgery. Reprinted from: *Ann. R. Coll. Surg. Engl.*, **23,** 213–237. 1958.

Collier (H. O. J.). Chemotherapy of infections. pp. 248. London: Chapman and Hall. 1954.

Durel (P.), and **Siboulet (A.).** Traitement des suppurations urétro-génitales et de leurs complications chez l'homme et chez la femme. p. 168. Paris: Doin. 1959.

Griffith (E. F.). Marriage and the unconscious. pp. 221. London: Secker and Warburg. 21s. 1957.

Hughes (A. W.). Nerves of the human body. pp. 32. Edinburgh: Livingstone. 1890.

Keynes (G. L.). Harvey through John Aubrey's eyes. (254th Harveian Oration, 1958.) pp. 23. London. 1958.

Rein (H.). Einführung in die Physiologie des Menschen. 8th ed. pp. 560. Berlin: Springer. 1947.

Ribeiro (L. P.), Mitidieri (E.), and **Affonso (O. R.).** Eletroforese em papel e métodos relacionados. Revisto G. G. Villela. pp. 553. Rio de Janeiro: I.B.G.E. 1958.

Società Italiana di Neurologia. Il problema dell'apoplessia cerebrale. pp. 243–428. Milan. 1952.

University College Hospital. Handbook. Incorporating the Handbook of clinical pathology. Editor: T. D. Whittet. pp. 130. Shrewsbury: Wilding. 1959.

Winkler (C.). Opera omnia. 10 vols. Haarlem: De Erven F. Bohn. 1918–1933.

BOOKS RECEIVED FOR REVIEW

Adriani (J.), and **Parmley (J. B.),** eds. The recovery room. pp. xii+123. Oxford: Blackwell. 32s. 6d. 1958.

Bailey (H.). Emergency surgery. 7th ed. pp. xvi+1197. Bristol: Wright. £9 9s. 1958.

Barber (H.). The rewards of medicine and other essays. pp. 140. London: Lewis. 15s. 1959.

Belisario (J. C.). Cancer of the skin. pp. xvii+321+14. London: Butterworth. 50s. 1959.

Bicknell (F.). Enuresis or bed-wetting. pp. 104. London: Heinemann. 7s. 6d. 1959.

Bigger (J. W.) Bigger's Handbook of bacteriology. Revised by F. S. Stewart. 7th ed. pp. x+611. London: Baillière. 37s. 6d. 1959.

Blackwell Scientific Publications 1959. Oxford. 1959.

Clyne (D. G. W.). A concise textbook for midwives. pp. 317. London: Faber and Faber. 32s. 6d. 1959.

Coërs (C.), and **Woolf (A. L.).** The innervation of muscle. A biopsy study. pp. xv+149. Oxford: Blackwell. 42s. 1959.

Collins (D. H.), ed. Modern trends in pathology. pp. x+334+12. London: Butterworth. 70s. 1959.

Crozier (T. H.). Aids to medical treatment. 4th ed. pp. 367. London: Baillière. 15s. 1959.

Dalsace (J.), and **Garcia-Caldéron (J.).** Gynecologic radiography. pp. xvii+188. London: Cassell. 60s. 1959.

Gebhard (P. H.), Pomeroy (W. B.), Martin (C. E.), and **Christenson (C. V.).** Pregnancy, birth and abortion. pp. xiii+282. London: Heinemann. 30s. 1959.

Hughes (E. S. R.). Surgery of the colon. pp. viii+415. Edinburgh and London: Livingstone. 63s. 1959.

Leibowitz (H. R.). Bleeding esophageal varices—portal hypertension. pp. xxxiii+986. Springfield, Ill.: Thomas. Oxford: Blackwell. £9 3s. 6d. 1959.

Manchester Committee on Cancer. Report on teachers' conference on cancer education, Lyme Hall, 14th–15th March, 1959. pp. 20. 1959.

MA5868 100

an attack of migraine has been averted...

'Stemetil' *trade mark* PROCHLORPERAZINE *brand*

for the prevention and management of true migraine

Detailed information is available on request

'Stemetil' is supplied as

5 mg. tablets

5 mg. and 25 mg. suppositories

1·25% solution for injection

MANUFACTURED BY M&B MAY & BAKER LTD

An **M&B** *brand Medical Product*

Distributors:

PHARMACEUTICAL SPECIALITIES (MAY & BAKER) LTD · DAGENHAM

Algipan*

the 'veteran' rubefacient aid to activity in muscular conditions

Economical 40 gramme tubes balm, 1.0% methyl nicotinate, 0.1% histamine dihydrochloride, 10% glycol salicylate and 0.1% capsicin.

Wyeth JOHN WYETH AND BROTHER LIMITED, CLIFTON HOUSE, EUSTON ROAD, LONDON N.W.1.

*trade mark

Alg 7

Section of Orthopædics

President—J. S. BATCHELOR, F.R.C.S.

Meeting
February 3, 1959

The Surgery of the Hip

PRESIDENT'S ADDRESS

By J. S. BATCHELOR, F.R.C.S.

London

THE surgery of the arthritic hip is in many respects a baffling problem for which we have yet to find a wholly satisfactory solution. In the years after the Second World War various arthroplasty procedures—the Smith-Petersen, the Judet and the Crawford-Adams—were employed with enthusiasm, but with disappointing results. Only the Smith-Petersen arthroplasty has survived, the other two having virtually disappeared. The tendency has been, therefore, to return to the older and better established procedures—arthrodesis, displacement osteotomy and pseudarthrosis—and it is these that I propose to discuss.

ARTHRODESIS

There is no general agreement on how best to achieve a bony ankylosis. There are five recognized methods:

(1) The Watson-Jones arthrodesis with joint erasion and internal fixation with a trifin nail.

(2) The McKee arthrodesis with joint erasion and internal fixation with a lag screw.

(3) The Pyrford arthrodesis, which is essentially a modified Watson-Jones procedure with, in addition, a subtrochanteric osteotomy.

(4) The Norwich "V" arthrodesis.

(5) The Charnley central dislocation.

Bony fusion.—Comments by Charnley (1953) on the Watson-Jones arthrodesis are disparaging—"before the operation the hip is like an orange inside a cup. After the operation it is like a peeled orange lying in a saucer", or "but even with internal fixation with a nail, and even where the denuded surfaces are reinforced with iliac bone, this arthrodesis still shows a strong tendency to fibrous union." Yet Watson-Jones and Robinson (1956), reviewing the results of this arthrodesis in 120 patients, reported bony fusion in 113 (94%), although it should be noted that 4 patients had 2 operations. A very important factor in the success of this method is undoubtedly the strict post-operative regime of sixteen weeks in a double hip spica. Although this long period of immobilization is not the great trial for the patient that some maintain, it might be possible to reduce it if some more efficient method of internal fixation were used. A carpenter would use a screw and not a nail to fix securely two pieces of wood. Difficulty is sometimes experienced in driving the trifin nail into the pelvis when the bone is dense and sclerotic, and when this occurs the femoral head and acetabulum may separate, producing a gap which cannot be closed, or the nail may refuse to advance even with heavy blows of the mallet, and may then prove very difficult to extract.

McKee (1957) also claims fusion in 94%, but 28% of his patients complained of some pain, and in only 66% was the result reported as good or excellent, and the screw fractured in 16%. His lag screw, however, has certain advantages, for it produces compression between the femoral head and the acetabulum which must help to provide secure fixation and assist bony union.

Mr. R. C. Howard has very kindly allowed me to read an unpublished report on the follow-up of a large series of Norwich "V" arthrodeses, some of which were performed by the late Mr. H. A. Brittain. The fusion rate in this series was 84%, but this figure may well be increased by technical improvements which have recently been introduced in the operation.

The report by Apley and Denham (1955) on the Pyrford procedure is presumably a preliminary one, for the series is small. In only 17 patients was an attempt made at arthrodesis combined with osteotomy. They state that in 2 patients the osteotomy took longer than usual to consolidate, and the short spica was retained up to five months from operation. My own experience of arthrodesis of the hip combined with osteotomy has been most unhappy. This procedure was performed on 2 patients for failed arthroplasty. In each patient the hip fused but the osteotomy failed to unite (Figs. 1 and 2). One patient accepted the pseudarthrosis; in the other repeated attempts were made to achieve union of the osteotomy, but without success. I believe that after internal fixation of the hip

FIG. 1.—Arthrodesis with intertrochanteric osteotomy (reinforced with iliac bone).

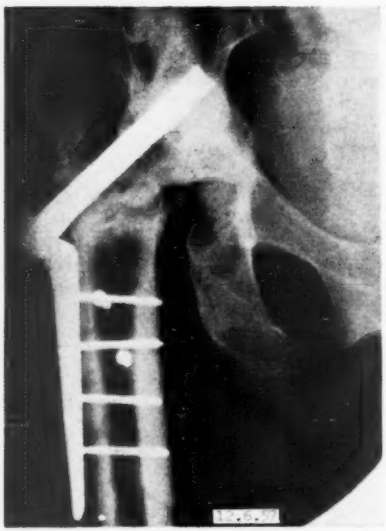


FIG. 2.—Non-union of the osteotomy.

failure of union of an osteotomy at this level is a real hazard.

Charnley (1953) with his central dislocation in his early series made no attempt to produce a bony ankylosis. He demonstrated that central dislocation is essentially a stabilising procedure producing in particular a block to adduction. He achieved excellent functional results in his first series of 44 patients, some of whom had a few degrees of flexion movements, others a fibrous ankylosis. Subsequently he attempted to achieve bony fusion by using spring compression, but it would seem that the success rate was not high, although he found that bony ankylosis sometimes occurred spontaneously two to three years after operation, or more certainly after osteotomy. In the course of the central dislocation operation as described by Charnley the head and neck of the femur are entirely deprived of their blood supply. This may be why bony union occurs so infrequently, and it may also be responsible for the spontaneous fracture of the femoral neck that has been reported. Furthermore, it would seem that bony fusion does not readily occur between the trochanter and acetabulum.

If the most reliable procedure at the present time for the arthritic hip is in most cases an arthrodesis, and I believe that many would agree, how can this best be achieved? The Watson-Jones procedure has a high proportion of bony fusions, but at a price which should not be required of each and every patient. Attention to certain technical details could, perhaps, improve the results by reducing for some the time spent in plaster and increasing the high fusion rate already achieved.

Medial displacement of the femoral head.—Bony union is most likely to occur when there is intimate contact between the cancellous bone of the acetabulum and the femoral head, and therefore burying the head in the pelvis is not helpful if bony ankylosis is desired. Some degree of medial displacement of the femoral head can often be achieved without attempting a central dislocation, and without unduly impairing the blood supply (Fig. 3). The stability is improved, fixation is more secure and there is maximum contact between the femoral head and the acetabulum. In congenital subluxation I have found that perforation of the acetabulum, as advised by Charnley, but taking care to preserve the blood supply of the upper end of the femur, is most useful.

Internal fixation.—A lag screw of the type used by McKee provides, I think, a more efficient form of internal fixation than the nail,

FIG. 3.—Arthrodesis of the hip with medial displacement of the femoral head. The nail is badly placed.

FIG. 4.—Oblique view of the ilium of a skeleton, showing the triangular area of bone above the acetabulum into which the nail is driven.

and would eliminate the difficulty already referred to when the bone above the acetabulum is dense. The direction in which it is introduced is important. When the head is displaced medially it should pass in the coronal plane through its lateral margin so as to engage the thick bone above the acetabulum. Little attention has been paid to the direction of the nail in the antero-posterior plane. Only Charnley gives any directions, advising that it should be introduced parallel with the floor. The triangular area of bone above the acetabulum is not large, and accurate insertion is essential if the maximum hold on the pelvis is to be achieved (Fig. 4). The nail or screw should be directed slightly backwards so that when it has been driven home its point will lie close to, or perforate, the brim of the true pelvis just below the sacro-iliac joint. Incorrectly directed nails will perforate the cortex anteriorly in the iliac fossa or posteriorly in the gluteal region. In a discussion on arthrodesis of the hip in 1939 Hindenach pointed out that an oblique X-ray of the ilium was required to demonstrate the true position of the nail.

THE MCMURRAY OSTEOTOMY

Surely this is one of the greatest enigmas of orthopædic surgery. During the last few years there have been many reviews of the results of this operation, and all report success in approximately 80% of cases. McFarland (1954), reviewing the results in a series of patients operated on by McMurray, stated: "to review at one sitting a series of old osteotomy patients is startlingly impressive"—and yet we cannot explain how these good results are achieved. McMurray (1939) recommended that "the lower fragment is displaced inwards until its upper margin lies directly under the cotyloid ligament of the hip-joint. If this displacement is not sufficient there can at best be only partial relief of symptoms, and a disappointing result". Malkin (1936) reported successful results following a trochanteric osteotomy to correct adduction and external rotation deformity in 12 patients with osteoarthritis of the hip. Osborne and Fahrni (1950) reviewed the end-results of 75 cases, and advised that "the distal fragment of the femur should lie in contact with the pelvis in such a manner that weight is borne through it". In 95% of their successful cases there was a block to adduction movement. Wardle (1955) reviewed 40 patients and advised that the upper fragment should be adducted and the lower fragment placed in the weight-bearing line. Adam and Spence (1958) in a review of 58 patients concluded that a good result could be obtained without medial displacement of the

distal fragment or correction of adduction deformity. But Holden, in a yet unpublished report, states that "the group of cases with minimal displacement had the highest proportion of failures except when they were accompanied by pre-existing adduction contracture".

The cause of pain in osteoarthritis.—Trueta (1954) believes that the symptoms of osteoarthritis of the hip are due to a hyperæmia of the proximal end of the femur and acetabulum, and the relief of pain following osteotomy is thought by some to be due to interruption of the blood supply to the femoral head. I doubt if this is a valid explanation. The aggravation of pain by excessive activity, the severe exacerbations produced by sudden strain or movement, and the gradual increase of symptoms as deformity increases and movement diminishes, and as subluxation develops, point to the soft tissues—the synovial membrane, capsule and ligaments—as the site of pain. In the terminal stages of the disorder, when joint movement is virtually abolished by osteophytosis and capsular contracture, pain may be relieved, as indeed it often is in arthritic joints elsewhere in the body.

The kernel of the problem is instability, which is a common cause of pain in other joints as well as the hip. It may produce symptoms long before there is radiological evidence of subluxation, and is, I believe, the chief cause of both the osteoarthritis and the subluxation. Incongruity of the hip from any cause, and dysplasia, make it potentially unstable, and although function may be satisfactory during early adult life troublesome symptoms develop when the effects of age, increasing weight and impaired muscle action are superadded. The damaging effect on articular cartilage of the abnormal movement produced by instability is seen in many situations: in the joint between the base of the first metacarpal and the trapezium in the hand, in the patello-femoral compartment of the knee, in the posterior joints of the lumbar spine in pseudo-spondylolisthesis and elsewhere.

The relief of pain by osteotomy.—It has been claimed that pain in osteoarthritis of the hip can be relieved by simple division of the bone without displacement, and without any particular attempt to correct deformity. When the upper end of the femur has been separated from the femoral shaft it is most unlikely that the two ever join again in their original position. Deformity may be corrected and pain relieved without obvious radiological evidence of a change of position. We tend to think only of flexion and adduction deformities, and to forget that correction of an external rotation deformity will also relieve strain. The immediate relief of rest pain after osteotomy may be due to relaxation of the strain imposed on the joint by the deforming action of the long femoral lever. When the osteotomy is carried out as advised by McMurray the stability of the joint is improved, and this is, I believe, the factor chiefly responsible for the relief of symptoms. I place the McMurray osteotomy with the many osteotomies of the upper end of the femur which are essentially stabilizing procedures.

Improvement in the radiographic appearance.—This has been commented on in previous reports,

FIG. 5.—Successful McMurray osteotomy. Note reformation of joint space. Fibrous union of osteotomy.

FIG. 6.—Osteotomy for ununited fracture of femoral neck. Good joint space, despite collapse of femoral head. No

and there is no doubt that it occurs, and that it is not merely a radiographic appearance as suggested by Arden (1957). Why it occurs we cannot yet explain, but it is found only in successful cases, and I believe it indicates that the joint has been stabilized and that articular cartilage responds to compression as opposed to sheering strains (Figs. 5 and 6).

Union of the osteotomy.—In my experience delayed or non-union is not uncommon, and the incidence may well be higher than is generally believed. Internal fixation is now in general use, and I find that difficulty with union is likely to occur when a method of fixation is employed which holds the fragments apart or prevents them falling together. A blade-plate is very satisfactory provided that the blade is driven through the cortex on the upper border of the trochanter or femoral neck. Strangely enough some patients in whom the osteotomy fails to unite have excellent function, but this cannot be relied upon.

Pseudarthrosis

The Girdlestone operation.—In 1938 Girdlestone introduced his pseudarthrosis by excision of the femoral head and neck. The instability that this produces renders it unsatisfactory as a routine procedure for osteoarthritis of the hip. Even when a weight-relieving caliper is worn for several months, and this is a most uncomfortable instrument for an adult, about two years are required before reasonable stability is achieved. After previous surgery or infection stability is acquired much more quickly, and it has therefore a useful place as a salvage procedure after joint infections or failed arthroplasty, particularly when the patient is light and has good muscle action.

The angled osteotomy.—I have found that stability is greatly improved by a subtrochanteric angled osteotomy. The combined procedure of excision and osteotomy has been performed as a two- or one-stage procedure. In the two-stage procedure the Smith-Petersen approach is used for excision of the femoral head and neck, and a fortnight later the osteotomy is performed through a posterolateral approach. In the one-stage procedure the operation is performed through an anterolateral approach between the tensor fasciæ femoris muscle and the gluteus medius and minimus. This gives good access to the hip-joint, and also, when extended distally, to the upper end of the femur. Resection of the head and neck should start just above the lesser trochanter and pass upwards and outwards along the intertrochanteric line. The cut surface of the great trochanter should be quite smooth, and osteophytes should be removed from the acetabular brim. Bony irregularities cause pain, and a revision operation may be needed to remove them.

The osteotomy must be performed one-half to three-quarters of an inch (12 to 18 mm.) below the lesser trochanter, and a locking osteotomy is used to prevent displacement. Judging the correct angle of the osteotomy is important and difficult: the best results are achieved when the distal fragment is abducted about 40 degrees, producing a block to adduction. Internal fixation is provided by an angled plate (Fig. 7). Post-operative treatment consists in Russell traction for six to eight weeks, and full weight-bearing is allowed when there is radiological evidence of union of the osteotomy.

I regard this operation as a salvage procedure, no longer using it as a primary method of treatment for osteoarthritis of the hip. I use it:

(1) After joint infection or failed arthroplasty, when a Girdlestone would give inadequate stability, particularly in heavy patients.

(2) In bilateral arthritis, when one hip has been arthrodesed, and the other hip is unsuitable for a McMurray osteotomy or formal arthroplasty.

(3) In unilateral arthritis when the changes present in the joint render it unsuitable for any of the formal procedures.

(4) In ankylosing spondylitis.

Bone-rubbing.—Trueta (1954) has suggested that the osteotomy produces bone-rubbing and

Fig. 7.

FIG. 8.—Successful excision-osteotomy, performed in 1942.

FIG. 9.—Unsuccessful osteotomy. Inadequately angled and a small weight-bearing area.

pain. This has not been my experience when the operation is correctly performed. The essential features are:

(1) Stability by adequate angulation.

(2) Distribution of weight over a wide area on the upper femoral fragment.

(3) Smooth bony surfaces (Fig. 8).

Many of my poor results are due to inadequate angulation of the osteotomy and weight-bearing on a limited area of the upper fragment (Fig. 9).

Duration of results.—I have found that the results of this operation improve rather than deteriorate with time. After some years sclerosis of the surfaces of the pseudarthrosis occurs, but this is not accompanied by pain. My early enthusiasm for this procedure was followed by a period of disappointment and doubt, but now I find cause for sober satisfaction with many of the long-term results.

Conclusion.—Arthrodesis is at the present time the most reliable procedure for the osteoarthritic hip, but, as Trueta (1954) has said, "it is a depressing reflection that the most effective treatment for osteoarthritis is still the elimination of the joint". Further study may tell us why the McMurray osteotomy succeeds, and enable us to use it more effectively. If it proves to be essentially a stabilizing procedure could it not be used more frequently as a prophylactic measure in order to avoid the gross degenerative changes for which only arthrodesis can be advised?

[A film of some long-term end-results following excision-osteotomy was shown.]

REFERENCES

ADAM, A., and SPENCE, A. J. (1958) *J. Bone Jt. Surg.*, **40B,** 219.

APLEY, A. G., and DENHAM, R. A. (1955) *J. Bone Jt. Surg.*, **37B,** 185.

ARDEN, G. (1957) *J. Bone Jt. Surg.*, **39B,** 750.

CHARNLEY, J. (1953) Compression Arthrodesis. Edinburgh and London.

GIRDLESTONE, G. R. (1945) *Proc. R. Soc. Med.*, **38,** 363.

HINDENACH, J. C. R. (1939) Personal communication.

HOLDEN, N. T. Personal communication.

HOWARD, R. C. Personal communication.

MALKIN, S. A. S. (1936) *Brit. med. J.*, i, 304.

MCFARLAND, B. (1954) *J. Bone Jt. Surg.*, **36A,** 476.

MCKEE, G. K. (1957) *J. Bone Jt. Surg.*, **39B,** 477.

MCMURRAY, T. P. (1939) *J. Bone Jt. Surg.*, **21,** 1.

OSBORNE, G. V., and FAHRNI, W. H. (1950) *J. Bone Jt. Surg.*, **32B,** 148.

TRUETA, J. (1954) *Ann. Surg.*, **15,** 174.

WARDLE, E. N. (1955) *J. Bone Jt. Surg.*, **37B,** 568.

WATSON-JONES, R., and ROBINSON, W. C. (1956) *J. Bone Jt. Surg.*, **38B,** 353.

more miles to the muscle with

Algipan*

the 'veteran' rubefacient aid to activity in muscular conditions

Economical 40 gramme tubes balm, 1.0% methyl nicotinate, 0.1% histamine dihydrochloride, 10% glycol salicylate and 0.1% capsicin.

Wyeth JOHN WYETH AND BROTHER LIMITED, CLIFTON HOUSE, EUSTON ROAD, LONDON N.W.1.

*trade mark

Alg.5

RIKER

there is no condition in which any degree of obesity is advisable

'. . . 25% of women attending their doctor are obese. These patients should be encouraged to reduce . . .'*

*Brit. (1959) 189, 226.

now dependable weight loss with

Durophet*

active appetite control without overstimulation

really long action: 12-14 hours from a *single* capsule

new ion-exchange release technique produces smooth, uninterrupted medication

new formulation: balanced amounts of dextro and laevo amphetamine (3 : 1 ratio) give more powerful appetite-suppressing effect, without increasing CNS stimulation

THREE strengths (20mg.; 12½mg.; 7½mg.) so that each therapeutic need can be met by prescribing a *single* capsule once a day. Containers of 30 capsules.

Riker Laboratories Ltd

Loughborough, Leicestershire

*Trade Mark RK

PARENTROVITE IN GENERAL PRACTICE

Parentrovite, a high potency injectable preparation of the vitamin B complex with vitamin C, is being found of increasing usefulness in general practice. Introduced originally for the treatment of acute psychiatric emergencies such as coma or delirium from alcohol or drug overdosage, it has since been found to be of much wider application for conditions not uncommonly met in patients being nursed in their own homes. Many a patient can now, with appropriate dosage, be kept at home instead of having to be admitted to a general or a mental hospital.

The formula is based on the fact that normal cerebral function depends on the oxidation of glucose and that any interference with the underlying biochemical mechanisms can cause symptoms of mental disturbance. Severe infections, burns, trauma, surgical operations and "stresses" of all kinds can be as potent as drugs and alcohol in causing interference with the enzyme systems responsible for glucose oxidation and resultant failure of return to health.

To reverse such changes and to restore normal cerebral function, massive doses of the B vitamins and ascorbic acid are needed—doses out of all proportion to normal nutritional needs. The vitamins are used here not as nutrients but as potent drugs employed pharmacologically.

Conditions Reported Responsive to Parentrovite

The after-effects of influenza, pneumonia and other severe infections,
Post-operative depression and confusion,
Debility with loss of memory in old people,
Alcoholism, acute and chronic,
Habituation to barbiturates.

Parentrovite

PACKS: in boxes of 3 and 12 pairs. Hospital pack also available.

Standard Reference Cards with factual information on all our products now available. Produced in accordance with the specifications of the Association of the British Pharmaceutical Industry. Our representative will be pleased to supply you with a complete set, or write to:-

VITAMINS LIMITED, UPPER MALL, LONDON, W.6.

Proceedings of the Royal Society of Medicine

Vol. 52
361

Section of the History of Medicine

President—Sir WELDON DALRYMPLE-CHAMPNEYS, Bt., C.B., M.A., D.M., F.R.C.P.

Meeting
February 4, 1959

Strafford—the Medical Background

By A. LESLIE BANKS, M.A., M.D., F.R.C.P., D.P.H.

Fellow of Gonville and Caius College, Cambridge

THOMAS WENTWORTH was born on Good Friday, April 13, 1593, in Chancery Lane, at the house of his maternal grandfather Sir Robert Atkinson, a bencher of Lincoln's Inn (Traill, 1889).

His father, William Wentworth, was a wealthy Yorkshire landowner, lord of two manors and descendant of a family which was deeply rooted in the West Riding. It was to Strafford's great-grandfather that Henry VIII granted the privilege of wearing his bonnet in the royal presence for "certain diseases and infirmities which he daily sustegneth in his hede". His mother was the heiress to her father's estate of Stowell in Gloucestershire. "Something less than a nobleman, something greater than a country squire, he (Strafford) belonged to that growing aristocracy of wealth who counted themselves inferior to none" (Wedgwood, 1935).

In 1593 Queen Elizabeth had still ten years of life before her. The defeat of the Spanish Armada was but five years old and the speech of the Queen in dissolving Parliament in that year displayed much concern at the activities of the King of Spain. The City of London was full of "lame, maimed, and poor creatures, going up and down the streets begging", and in April 1593 the butchers of the City were in trouble for not supplying these maimed soldiers with meat.

It was a time of extremes of wealth and poverty. The few ate and drank to excess and the rest went hungry when corn and meat were short. The masses were illiterate, and accustomed to brutality.

Only twenty years had elapsed since the death of John Caius, worn out at the age of 62 with the struggles with the Fellows of his College, Puritans to a man. When they ransacked the Master's Lodge for his "massing abominations" Caius retired to his house in London "much grieved and disturbed at the furious and rash zeal of those times". Coming events were indeed casting their shadows before them (Venn, 1901).

Some six weeks after the birth of Strafford another great physician, William Harvey, was admitted to the scholar's table at Caius, at the age of 16. By the time of his death, in 1657, nearly all the principal actors in the great drama had died, many by violence. It is fortunate for us that Harvey cared little for politics, as his letter to John Nardi showed (D.N.B., 1891).

Strafford was beheaded on May 12, 1641, and few men can have crowded such intensity of effort into such a short span of years, or aroused such bitter animosity. Intelligent, sensitive, a brilliant administrator, yet he became "Black Tom Tyrant" whose death was the most sought-for object of the peoples of England, Scotland and Ireland. He could not, and must not, be allowed to survive, for "stone dead hath no fellow". The cry that "His head is off! His head is off!" gave rise to a frenzy of jubilation throughout the length and breadth of the kingdom.

Clearly it is of great interest to enquire further why this man, who could trace his pedigree to John of Gaunt, and with such a long family tradition of public service, should have failed. True, he had a master of whom Archbishop Laud was to write sadly that he "knew not how to be, or be made, great". On the other hand Charles had good reason to write, in his "Eikon Basilike", that "I looked upon my Lord of Strafford as a gentleman whose great abilities might make a monarch rather afraid than ashamed to employ him in the greatest affairs of State". His fears were well-grounded, for it was indeed Strafford who counselled the King on the final extreme measures preceding the summoning of the Long Parliament.

Where then did the fault lie, with the King, the Minister, or the times? I think the verdict must be that given by Wedgwood, on Strafford,

"Mentally, as physically, he was betrayed from within" (Wedgwood, 1935).

It all began so promisingly. Educated at St. John's College, Cambridge, and the Inner Temple, he had the ability, as he humorously admitted, to make himself appear more widely read than in fact he was. At the age of 18 he was presented at Court by his father, who had just purchased a baronetcy from James I. This new hereditary dignity was obtainable at a fixed tariff per head of £1,080, payable in three annual instalments, the money to be used to complete the settlement of Ulster. In the same year, 1611, a marriage was arranged with Margaret Clifford, daughter of the Earl of Cumberland, and six weeks later Strafford was knighted by the unsteady hand of the King, at Royston. He was, be it noted, only 18 and he had not yet completed his education. Accompanied by a tutor he bade farewell to his wife and toured Europe for fourteen months. On his return, and before his twenty-first birthday, he took his seat in the Addled Parliament as member for Yorkshire. In that year, 1614, his father died, leaving him an income of £6,000 a year and the guardianship of nine children not yet of age, in addition to the two young children of his elder sister Ann, who were also his wards.

Already he was showing signs of a violent temper, quickly roused and difficult to control, together with that meticulous attention to detail which was to become obsessional. Also becoming evident was the pleasure and familiarity he showed in the company of his inferiors and which was later to be a source of irritation to his peers, who could not understand why he preferred a pipe of tobacco with his steward to dining abroad.

His simple habits, also, puzzled his neighbours, for, although he could and did entertain on the grand scale in his official capacity, he preferred raw fruit and country dishes for himself, and his statement that he had never been drunk in his life was received with scepticism. He was not interested in sport, with the exception of hawking and fishing, and his shy nature was soon to become hidden in public by a harsh, forbidding, and overbearing manner. Perhaps his greatest innate weakness was this extreme sensitivity, for he never succeeded in acquiring the pachydermatous covering so essential in public life. Criticism hurt unduly, and led him to withdraw from the everyday contacts so necessary at a time when the conduct of affairs might require to be adjusted at a moment's notice.

The melancholy side of his nature, later to be revealed in moods of the deepest depression, may be divined from his early portraits. Tall, stooping, thin, with jet-black hair cropped short, heavy black brows under a high forehead, and with piercing dark eyes set in a face "as white as a candle", he has the appearance of a man of deep emotions. The tightly compressed lips, set expression, and jutting lower jaw complete the portrait. Clearly, this was a man of great potentialities. The way in which the stoop increases, and the lines of tension appear in his later portraits, together with the sadness and apprehension in the eyes, is painful to observe.

At first all went well. The Yorkshire squire became, at 22, head of the Commission for the Peace in the West Riding. At 26 he was elected a member of the Council of the North, the judicial and administrative body corresponding to the Court of Star Chamber in London. Unfortunately his nature would not let him rest content. "In all things distrusting himself" he must press on to London and seek higher honours. Twice at least he negotiated unsuccessfully for a peerage.

It was not long before he had aroused feelings of detestation. Old Lord Powis, after listening to his dissertation on the length of his pedigree, was heard to say "Damme, if ever he comes to be King of England I shall turn rebel."

There was no question, however, as to his ability, and increasing experience might have remedied much, but in 1622 came the first major setback, with the death of his wife and the first record of his many illnesses. In his own words:

"Myself having been dangerously sick of a pestilent fever removed the 29th July 1622, from Austin Friars in London (where I remained during my sickness) for fresher air to Stratford upon the Bow. On Thursday following at night being the second of August 1622 this blessed lady's sickness began with a vehement casting and purging which continued till Friday morning about 3 o'clock. Then there came upon her an extraordinary shaking by the space of two hours wherein, notwithstanding she rather felt heat than cold, next after a little slumber she awaked and fell into an extreme burning which continued some three hours. Both which fits were so violent as she affirmed never to have been so ill in her life. After her burning she sweat some three hours very much. Nevertheless her distemper of heat still remained with a shortness and difficulty of breathing so as she could take no rest. On Sunday morning she had taken from her eight ounces of blood which albeit passing black yet otherwise was not very corrupt. . . . Whereupon I walking in her chamber (on Tuesday morning) she called me to the bedside and told me with weeping tears, fearing it would discomfort me (as I imagine), that she had a suit to make to me which she must not be denied, desiring she might move it unto me without offence. . . . I pray you, then said she, let Mr. Mackernesse be sent to and

desired that he will to-morrow by seven of the clock come hither and administer unto me the Communion for in diseases of this nature I know it is ordinary for people to lose their sense. And therefore I dare not trust myself till Thursday being the critical and seventh day of my sickness."

(She made her confession, lamenting her pride.)

"The next day being Thursday the seventh and critical day of her sickness there were good signs of amendment so as the physicians were persuaded the danger was past, yet she told Dr. Matthias that very morning that they lost their labour, for she was sure she must go to her good God."

She grew worse on Sunday morning, despite more bleeding and the application of hot pigeons to her feet "to draw down vapours from the head". He describes how he prayed with her at intervals throughout the Sunday, until her death early on Monday, as he read aloud the Visitation of the Sick.

Strafford retired to Yorkshire where he remained shaken by his loss and by recurring bouts of ague. From now onwards his stormy career mounts, and so also does the record of his illnesses. On the day of his second marriage, in 1625, his steward, Marris, noted that "Sir Thomas Wentworth was much afflicted on the day with a fit of the stone and bloody vein [*sic*] . . . at night it left him". His bride, the beautiful Lady Arabella Holles, was 16. He was now 32.

Then came two events of decisive importance. He was publicly humiliated by Buckingham, and later committed to the notorious Marshalsea Prison "in the height of summer and with plague about" for refusal to pay a forced loan to the King. This was succeeded by enforced detention at Dartford for some months. The result was inevitable with a man of his temperament. When Parliament met in March 1628 he became the leader of the opposition to Buckingham and the King, and champion of the Petition of Right. "They have taken from us,—what shall I say? Indeed, what have they left us?" set the tone of his speeches. It soon became evident that, with a man of such courage and gifts of oratory in opposition, both Buckingham and the King himself were in danger. Charles acted quickly. A month after the prorogation of Parliament Wentworth was created a baron and the "northern lad, baron of I know not where" became the fallen archangel of the people. At one stroke he became the most hated man in England, after Buckingham.

As a Privy Councillor, however, he was no more successful socially than as a courtier. He sat uneasily at the board drawing unflattering faces, "Vandyking", in Secretary Windebanke's words. He travelled incessantly between Yorkshire and London but during the plague of 1630 he and his family remained in York to reassure the townsfolk, and his youngest son was buried by night in York Minster in order to conceal the loss of the Lord President of the North.

Then came the greatest blow of all. His wife, to whom he was passionately devoted, was expecting her fifth child. One morning he came in from the garden to speak to her. An insect on his coat flew suddenly in her face, she stepped back, tripped, fell, was prematurely delivered of a stillborn child, and died. She was 22. His "saint in heaven" had gone, and to add to his misery his wife's family blamed his carelessness for her death. The shock was so great that he could not be left, night or day, and for many weeks he was shut in his house.

There was only one relief left, to work. First as Lord President of the North and then as Lord Deputy of Ireland he forged the adjective "thorough". It is difficult to visualize the magnitude of the task confronting him in Ireland, but some indication of the unsettled times is given by the fact that three pirate ships were on the look-out for him off the Welsh coast, and one, the *Pickpocket of Dover*, succeeded in capturing his linen. It was "but a cold welcome to that coast", as he said.

Ireland was in the hands of a clique of self-seeking Protestant landowners, of whom the chief was Richard Boyle, Earl of Cork, of whom the Lord Bishop of Waterford had complained that he had often heard of bishops being burnt to death in martyrdom, "but of a Bishop Boyled to death, never before". To subdue these men and restore law and order was a formidable task, and it was not long before Wentworth was writing to Laud to say, "I am desirous to rest myself but it must not be . . . how I shall be able, thus tired, to get through the Lord knows". His fits of depression increased, and in 1635 his constitution gave way. His hands, feet and one knee were crippled with gout, he had periodical bouts of headache and sleeplessness, together with intermittent attacks of the stone. One evening he fainted twice while going to bed, and on at least one occasion he was reported dead.

He was now 42 and physically and mentally exhausted. His children by his third wife, whom he had married secretly within a year of his second wife's death, were delicate and ailing, and not expected to live. He wrote at this time "I grow extremely old and full of grey hairs . . . Remember I tell you I am of no long life".

In his conduct of public affairs he became increasingly high-handed, and he was tormented

also by the realization that the King did not trust him. Indeed his only friend at Court was Archbishop Laud. Each new effort took its toll. After his tremendous speech at the opening of the Irish Parliament in 1634 he reeled and almost fainted, and was ill for three days after. He now had confidence in no one and even worked out the figures of his ciphers himself in order that his secretary, Sir Philip Mainwaring, should not know the key.

In May 1635, he wrote to his steward Marris "I have had a long fit of the gout. Am lame still and write this lying in a manner all along, which makes me scribble in this abominable manner as you see," and a little later he told Laud that the continual sitting and lying had brought on a disposition to his ancient acquaintance, the stone, "which a gentle trotting horse this journey hath, I hope, shaken quite asunder and carried away in great quantities of gravel". Two months later he was complaining that his head continually fell to aching as soon as he took a pen into his hand.

It is possible that his self-pity was at this time aggravated by the charges that he was feathering his own nest in Ireland, and also by the King's cold refusals to grant him an earldom. His temper, never fully under control, began to betray him. When a page toppled a stool on to his gouty foot he struck him with his cane. By an unhappy chance the boy was a relation of Lord Mountnorris, who was already smarting under a similar incident when Wentworth had brought his cane across the shoulders of his brother, Lieutenant Annesley, during a review of the Army. So hotly were the passions of the Annesleys aroused that Wentworth's friends feared for his life.

Wentworth's reputation for ruthlessness was now reaching its peak, and Laud began to grow anxious, but his physical ailments had begun to take charge. In May 1636 he had an attack of the stone "above anything I endured since I was a man". Meanwhile he had serious domestic worries. His three elder children were always delicate, and in addition two sons and a daughter, born in Ireland, followed each other in quick succession to the vaults of Dublin Cathedral. His two favourite sisters and three of his brothers also died while he was in Ireland. It is not surprising that he found that he had "more choler than at all times (he) was able to govern and control". His extremity of temper began to manifest itself in his despatches to the King, who must now show himself to be strong in dealing with the gathering disaffection. "Less than thorough will not overcome, there is a cancerous malignity in it which must be cut forth. This evil grows from a universal distemper of the age."

The attacks on Wentworth mounted from all directions. In the midst of dealing, from Dublin, with the intrigues against him by the Queen's party he had to answer the rumour circulated by the Earl of Holland that he was a lunatic and had been shut up in Bedlam for three-quarters of a year. When challenged Holland immediately withdrew. He had never, he said, indicated more than that the Deputy was a little given to hypochondria. Wentworth's illnesses were so well known that the retraction "turned the laugh against him with a vengeance" (Wedgwood, 1935). Next came a libel action against Sir Piers Crosby, Lord Mountnorris, and others, which was successful, but only at the price of more enemies. Even the King must have got a little tired of learning from his letters that he was so wracked with toothache that he could scarcely write. It must also have seemed odd to the army in Ireland to see their commander-in-chief carried on to the field of review day after day because he was unable to stand.

Then, on August 5, 1639, came the message which was to herald a brief Indian Summer. "Come when you will, ye shall be welcome to your assured friend, Charles R."

The King was, by now, at the end of his tether. He had completely misjudged the Scots, whose country he had only visited once and had become involved in what was, in effect, a religious war. There was only one man left to whom he could turn. For Wentworth the summons was what he had wanted for so long. Now he could leave Ireland to become the Chief Minister of State. It came, however, too late, for his physical and mental powers were much reduced. That night he slept badly, and another attack of gout crippled him so that he could hardly stand. His eldest son also was seriously ill and must be left behind with his wife, newly delivered of a daughter. Above all was the knowledge that everything depended on him and that he stood alone. "The nearer I come to it", he wrote, "the more my heart fails me; nor can I promise myself any good by this journey. God's will be done!"

In September 1639 he sailed from Dublin. At first all was well. The coveted earldom was at last granted, together with the splendid title of Lord Lieutenant of Ireland, but his judgment was becoming faulty. Even in the choice of his new title he gratuitously insulted Sir Henry Vane by choosing to be Baron of Raby, an estate which Vane himself owned. More serious was his failure to understand the Scots and their Covenant. From the

moment that he decided in 1640 that they were merely rebelling "for ceremonies, for things purely and simply indifferent" his fate, and that of his Royal master, were sealed.

The gout was now a major enemy, for he had to travel back to Dublin for the opening of the Irish Parliament in the Queen's own coach drawn by six horses, in thirteen agonizing stages, and he was reduced to the sad little jest "what might I be with my legs that am so brave without the use of them". He had not been in Ireland a week before he developed dysentery so severely that he was prostrated and his doctors advised him not to return to England. He wrote to the King "that which troubles me above measure is my present indisposition, for besides my gout I have a very violent and ill-conditioned flux upon me such as I never had before. It hath held me already these seven days, and brought me so weak, as in good faith nothing that could concern myself should make me go a mile forth of my chamber".

Nevertheless, he had himself conveyed in a litter on board a pinnace and forced the captain to put to sea in the teeth of a raging gale. Violent sea-sickness for a night and a day added to his misery and then on landing he felt the warning pain of gout in his other foot. So ill was he that the King sent a personal message "to command you not to hazard to travel before ye may do it with the safety of your health".

Strafford had now, in my view, passed the bounds of normality. Even on his slow journey back to London he was sending fierce messages ahead—"fall on the transgressors like lightning"—"clap Lord Loudon in prison without delay"—"give the gentlemen something to remember hereafter", and so on.

He arrived in London on April 18, 1640, utterly worn out. Parliament was already in session, with Pym as the leader of the Commons. Once again the King dismissed them. The kingdom was now in an uproar, and the one man who might have steadied the panic-stricken Council was so exhausted by dysentery and the merciless blood-letting of his physicians that he could not stand, and he developed pleurisy. The City of London had refused to supply the King with money. "Have at them", cried Strafford in a fury, "Whip them into their senses." Such was the mental and physical condition of the man who now travelled north to assume supreme command of the Army against the Scots. On the first stage of that journey he reached Huntingdon, where he sat sleepless with a relapse of dysentery and severe pain on breathing.

At York a sudden attack of the stone sent him grovelling and his life was feared for. He was in bed when the defeated stragglers arrived from the debacle at Newburn. He rose and marched to Northallerton with his forces. There he had another attack of the stone and his self-control finally failed. In a black fury he fell upon the inefficient army, with wholesale arrests, hangings, and shootings. "Have at them—set up a gallows and a horse before each regiment to show them what will happen to those who disobey or mutiny now." It was too late. A humiliating settlement with the Scots, and the summoning of Parliament, were inevitable. Once more Charles called him to London. It was then that Strafford wrote "I am tomorrow to London, with more danger beset, I believe, than ever man went with out of Yorkshire, yet my heart is good and I find nothing cold within me".

The rest of the story is too well known to require repetition. The Long Parliament had begun, and Pym was moving fast. When Strafford left the King at full gallop for the Lords at Westminster he found Pym already there, with the impeachment of the Commons of England accusing Thomas Wentworth, Earl of Strafford, of high treason. He was committed to the Tower, where he remained for two long winter months while the charges were formulated against him. When he emerged "pale and stooping" to learn the nature of those charges he was jubilant, for his keen mind detected their flimsy nature.

Nothing in his history is more characteristic of his indomitable spirit than the way in which, day after day, he met the onslaught of his prosecutors. It was a discreditable scene. Members of the Lords and Commons walked about and joked and chattered. Food and drink circulated freely and the calls of nature were answered by the people remaining in their places, merely turning their backs to the King and Queen and the noble ladies in the gallery.

No one, so far as I am aware, has ever questioned Strafford's courage or intellectual ability, and his conduct at his trial drew tributes from his most bitter opponents, including the "Scotch Commissioner" Robert Baillie. His final speech lasted more than two hours and was one of the most powerful of his career. After it he walked up and down in the Tower "in high spirits, even singing psalms of thanksgiving". But "stone dead hath no fellow" and die he must, so at once the Commons introduced the Bill of Attainder. It is only fair to Pym and his colleagues to say that by now they had no alternative. The whole country, to say nothing of the Scots, was clamouring for his death, and the machinations of the Queen and

her party were giving rise to the wildest rumours of Catholic uprisings and Spanish invasions. Sir John Coke, Secretary of State, although shocked beyond measure at the way the House of Commons was prepared to condemn a man to death by amending the law to create a crime after its commission, concluded, "so that unless this Earl be sacrificed to the public discontentment, I see not what hope we have of peace."

It remained, however, for the King himself to decide the issue. He determined to tell the assembled Parliament of England that his conscience could not agree to the condemnation of Strafford. "My Lords", he said, "I hope you know what a tender thing conscience is: yet I must declare unto you that to satisfy my people I would do great matters; but this of conscience, no fear or respect whatsoever shall make me go against it"—a well-meant, courageous, and fatal declaration. Nine days later he signed the warrant for Strafford's execution. All his promises to his minister came down, in the end, to the pathetic little postscript "If he must die, it were charity to reprieve him till Saturday".

Strafford died, as he had lived, fearlessly. Born plain Thomas Wentworth he had, in forty-nine years, become Earl of Strafford, Lord Lieutenant of Ireland, Lord President of the North and Lieutenant-General of the King's forces. In this brief paper I have tried to show how his recurrent and painful illnesses combined with his moody and uncertain temper to bring about his downfall. The English have always mistrusted the able administrator who lacked the common touch, and as Clarendon said "It was his misfortune to be of a time wherein very few wise men were equally employed with him, and scarce any whose faculties and abilities were equal to his".

Some indication of the orderly fashion of his mind may be gleaned from the headings for his last speech on the scaffold, taken from a paper that fell from his bosom after his death:

1. Come to pay the last Debt we owe to sinne.
2. Rise to Righteousnesse.
3. Dye willingly.
4. Forgive all.
5. Submit to justice, but, in my intentions, innocent from subverting etc.
6. Wishing nothing but good prosperity to King and People.
7. Acquit the King constreined.
8. Beseech to repent.
9. Strange way to write the beginning of Reformation and settlement of a Kingdome in blood.
10. Beseech that demand may rest there.
11. Call not blood on themselves.
12. Dy in the Faith of the Church.
13. Pray for it, and desire their Prayers with me.

It only remains to quote the poem circulated as a broadsheet in the summer after his death:

> "Here lies wise and valiant dust
> Huddled up 'twixt fit and just,
> Strafford, who was hurried hence
> 'Twixt treason and convenience.
> The prop and ruin of the State;
> The People's violent love and hate;
> One in extremes, loved and abhorr'd.
> Riddles lie here, or, in a word
> Here lies blood, and let it lie
> Speechless still, and never cry."

Wise and valient dust, riddles lie here indeed.

Acknowledgments.—I have drawn freely on the biographies by Wedgwood, The Earl of Birkenhead, and Traill. I have also read various tracts and pamphlets of the period in Caius College library, especially the writings of John Rushworth, who was present at the trial, and also Fuller's "Worthies".

I am indebted to Mr. W. K. Pyke-Lees, Mr. P. Wade of the Royal Society of Medicine Library, Dr. Llywelyn Roberts, and Sir Arthur MacNalty for their help and advice.

I understand that there is still much unpublished material concerning this remarkable man.

REFERENCES

BIRKENHEAD, THE EARL OF (1938) Strafford. London; p. 42.

D.N.B. (1891) Dictionary of National Biography. **25,** 98.

TRAILL, H. D. (1889) Lord Strafford. London; p. 2.

VENN, J. (1901) Biographical History of Gonville and Caius College. Cambridge; **3,** 54.

WEDGWOOD, C. V. (1935) Strafford. London; pp. 15, 219, 347.

GLAXO

antibiotic development of great promise

GRISOVIN

(griseofulvin Glaxo)

The first oral treatment for fungal infections of the skin

Systemic therapy of fungal infections of the skin has long been recognised to be the desirable form of treatment. It can now be achieved orally with griseofulvin, an antibiotic developed by Glaxo.

GRISOVIN TABLETS

Tablets containing 250 mg griseofulvin

Basic N.H.S. cost in the United Kingdom:
Bottles of 100 — 60/- each. Bottles of 1000 — 560/- each

GLAXO LABORATORIES LTD, GREENFORD, MIDDLESEX BYRon 3434

Subsidiary Companies or Agents in most countries

GRISOVIN IS A GLAXO TRADE MARK

NEW ANTIBIOTIC PRODUCTS FOR TOPICAL APPLICATION

For the treatment of the combined picture of reaction and infection, whichever is the primary element

Framycort

LOTION

Combined steroid-antibiotic therapy. Antibacterial, anti-inflammatory, antipruritic.

CHIEF INDICATIONS

Otitis externa
Anogenital pruritus
Seborrhoeic dermatitis
and all cases where infection complicates the eczema-dermatitis group of reactions.

PRODUCT	FORMULA	PACK	BASIC N.H.S. COST
Framycort	framycetin sulphate 0.5%, hydrocortisone acetate B.P. 0.5%	20 ml.	9/6
Framygen	framycetin sulphate 0.5%	1½ G.	1/-

ALSO

Framygen

— A STRAIGHT ANTIBIOTIC CREAM

CHIEF INDICATIONS

Otitis externa
Impetigo
Sycosis barbae

GENATOSAN LIMITED, LOUGHBOROUGH, LEICESTERSHIRE

Section of Dermatology

President—JOHN T. INGRAM, M.D., F.R.C.P.

Meeting
November 20, 1958
(contd. from March *Proceedings*, p. 192)

Erythema Gyratum Repens (Gammel, 1952).—J. SCHNEEWEISS, M.B. (for S. C. GOLD, M.D., F.R.C.P.).

Mr. F. M., aged 61. Painter's labourer.

History.—22.6.58: Piece of scaffolding fell on right forearm, causing multiple abrasions. No local medication was applied at the time. Several days later itchy rash appeared at the site of the injury, which soon spread to involve arms and trunk.

Over the next few weeks he was treated by means of antihistamines, calamine lotion and calcium gluconate tablets, a toxic erythema of unknown origin having been diagnosed.

There was no improvement in his condition, which became more widespread, the pruritus being most intense. His skin would become exceedingly dry, each area shedding a few days later to reveal gyrate areas of erythema of a bizarre pattern, the lesions slowly changing day by day (Fig. 1).

FIG. 1.—Back of trunk and arms showing generalized gyrate erythema with marginal desquamation.

He was referred to the Hammersmith Hospital on 2.9.58, at which time both his arms and trunk were involved, showing gyrate erythema in irregular wavy bands with marginal desquamation.

He had not had any previous illnesses or skin eruptions. He has been a heavy smoker for over forty years.

Investigations.—E.S.R. 2 mm. in one hour (Westergren). Full blood count normal. Chest X-ray normal. Skin biopsy: non-specific inflammatory reaction.

Management.—Prednisone, antihistamines, dapsone, soothing lotions, extraction of septic teeth.

In the absence of any response to this treatment, he was admitted to hospital on 15.10.58 for further investigation.

Further investigations.—E.S.R. 8 mm. and 7 mm. in one hour (Westergren). Full blood count normal on two occasions. W.R. and Kahn negative. Liver function tests, acid phosphatase, blood urea and anti-streptolysin-0 titre all normal. Sternal marrow normal, no evidence of reticulosis.

Serum proteins: 20.10.58, total 6·9, albumin 2·8, globulin 4·1 grams/100 ml. 4.11.58, total 7·1, albumin 3·5, globulin 3·6 grams/100 ml.

No L.E. cells. Fæces: no occult blood. Sigmoidoscopy: no abnormality seen. Barium meal: small hiatal hernia present; no other abnormality.

By this time his weight had gone down from 10 st. 13 lb. to 9 st. 12 lb.; a few small soft discrete glands could be palpated in each axilla and there was slight finger clubbing.

Chest X-ray (22.10.58): A change was now apparent in that there was some thickening of the horizontal fissure. Tomography of the hilar regions was then carried out and this was reported as demonstrating "enlargement of the right hilum with some central calcification within it and also marked thickening of the horizontal fissure. The appearances are suspicious of a bronchial neoplasm even although the major bronchi appear patent. Note the narrowing of the trachea above the level of the aortic knuckle. This may indicate the presence of lymph nodes."

Bronchoscopy (Dr. P. Hugh-Jones) 3.11.58, under local anæsthesia: "Bronchoscopy appearances suggest bronchial carcinoma affecting right upper and probably right main descending bronchus. Anterior enlargement of carina sug-

gests that there is likely to be glandular involvement and the growth would appear inoperable."

Biopsy report.—Infiltration of the bronchial mucosa with plasma cells and lymphocytes is seen. One area shows squamous metaplasia with some activity of the cells but no definite evidence of malignancy.

Progress.—He was seen in consultation by the thoracic surgeon and thoracotomy was not considered justified. On 12.11.58 he began supervoltage therapy on the linear accelerator, his supposed primary and mediastinal gland areas being irradiated. To date there has been no improvement in his skin condition which has in fact spread further to involve his legs and face, his entire skin thus being affected.

Dr. Stephen Gold: This rather curious eruption is presumably associated with the development of a bronchial carcinoma, but there were two clinical points, namely a normal sedimentation rate and a normal chest film, which were against such a diagnosis in the first place. It will remain to be seen what happens to this eruption once his present course of radiotherapy has been completed.

Within the last few months I have followed another patient, a man of 65, who developed a pemphigoid type of eruption, and this also was associated with a pulmonary neoplasm. The eruption, which consisted of gyrate erythema with a development of subepidermal blisters, mostly arranged at the periphery of the erythematous patches, was unresponsive to dapsone but was virtually controlled by oral corticosteroids. It was intensely irritable.

I believe these bullous reactions associated with visceral neoplasms to be not particularly uncommon; their mechanism of production, however, can only be speculative.

POSTSCRIPT.—7.1.59 : Patient completed a radical course of supervoltage radiotherapy on 12.12.58 directed to the right anterior and left posterior thoracic fields. There was no significant alteration noted in the appearance of his skin condition, but there was considerable reduction in pruritus. Tomography on 1.1.59 showed a decrease in size of the right hilar mass. However, considerable narrowing of the trachea just above the level of the aortic knuckle was still apparent.

19.1.59: He was presented to the Section again, the skin being now virtually clear of rash. He was free of itching and had gained 7 lb. in weight.

10.3.59: Skin now completely normal. Only symptoms are slight unproductive cough and minimal dyspnœa. Chest X-ray shows no further significant change.—J. S.

REFERENCE

GAMMEL, J. A. (1952) *Arch. Derm. Syph., Chicago*, 66, 494.

Alopecia Mucinosa (Pinkus).—C. J. STEVENSON, M.D.

Mrs. P. C., aged 25. Housewife.

History.—Nine years ago, some months after recovering from erysipelas of the face, she developed an itching rash on the forehead, starting on the right eyebrow. She was given X-ray (75 r × 3) to the affected areas, six years ago, with temporary benefit. A year later the condition had progressed to involve the left cheek and right nostril; a new lesion also appeared over the right posterior axilla. A year ago the tips of the shoulders became affected and itching papules developed on the lateral aspect of the elbows. Similar itching papules appeared on the buttocks during the past six months.

Her present and past health has been good.

Clinical findings. — Indurated erythematous plaques with some superficial scaling and excoriation are present over the eyebrows, forehead, the left cheek, the region of the right nostril and the chin. There is partial alopecia of the eyebrows. The hair follicle ostia are patulous. Similar plaques over the tips of the shoulders, and one over the posterior aspect of the left axilla, show multiple follicular spinous processes. On the elbows and buttocks are a number of excoriated papules.

Histology (Dr. H. Haber).—One follicle shows a characteristic mucinous degeneration of its wall. Diagnosis: Alopecia mucinosa (Pinkus).

Dr. Henry Haber: Since Pinkus (1957) described alopecia mucinosa, the concept of this condition has changed. It has been shown by Braun-Falco (1957) that follicular mucinosis can appear both as an idiopathic disease of follicles,

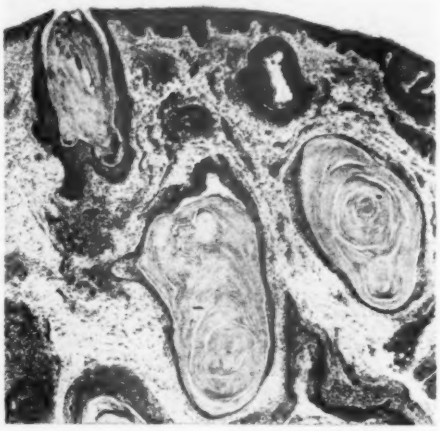


FIG. 1.—Dilated follicles filled with keratin, spongiosis and mucin within the walls of follicles. × 20.

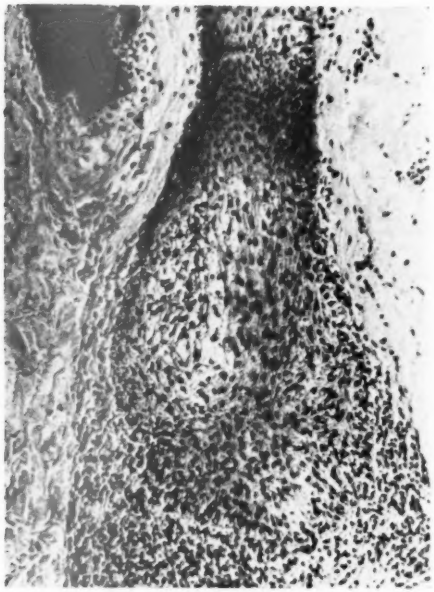


FIG. 2. — Hyperplasia of follicle showing "spongiosis" with the presence of mucin and a marked round cell infiltration. × 105.

FIG. 3.—Detail of Fig. 1. × 295.

and as a symptomatic follicular mucinosis accompanying reticulotic processes.

This case shows further histological features of the condition not described hitherto. When a biopsy of a lesion of the face was taken the histology showed the presence of numerous follicular cysts filled with concentric keratin masses lying within the corium, heavily infiltrated with inflammatory cells. Serial sections revealed the "cysts" to communicate with follicular openings, plugged with keratin (Fig. 1). No definite histological diagnosis could be offered at the time. When Dr. G. C. Wells suggested that the case might be alopecia mucinosa a second biopsy of an axillary lesion was performed.

The histology confirmed Dr. Wells' diagnosis. Several follicles showed the typical histological appearance of follicular mucinosis, as described by Pinkus. There was a marked perifollicular infiltration; the follicles showed hyperplasia and focal mucinous disintegration. Alcian blue showed the presence of mucin (Fig. 2). The first section was then reviewed and the follicular cysts revealed several foci of spongiosis in their walls which on staining with Alcian blue showed the presence of mucin (Fig. 3).

There is no doubt in my mind that the histological appearances I have just described represent both ends of a dynamic process occurring in follicular mucinosis. At the beginning there is mucinous degeneration of the follicles. At this stage the condition may clear up without sequelæ. If, however, the condition goes on and becomes chronic, then the follicles undergo hyperkeratosis with cystic transformation.

I remember a case of Dr. I. Muende's. He was a man of about 60 who showed a peculiar alopecia of both eyebrows with milia and swelling and redness of the skin (Fig. 4). At

FIG. 4.—Alopecia of eyebrows and milia formation.

this time he was diagnosed as ulerythema ophryogenes. I reviewed the slides and found the same histology as seen in Fig. 1. Stain for mucin revealed its presence in follicular walls. There is no doubt that this case represents a chronic stage of alopecia mucinosa.

Further study of this condition is indicated to establish the true nature of it. One should, perhaps, look out for cases of spinulosis to see whether they belong to this new dermatosis.

REFERENCES

BRAUN-FALCO, O. (1957) *Derm. Wschr.*, **136,** 1289.
PINKUS, H. (1957) *Arch. Derm. Syph., Chicago,* **76,** 419.

Dr. I. Martin-Scott: My case of alopecia mucinosa has done well without X-ray or other treatment. The condition was present for a total period of one year, and has now completely disappeared.

The following cases were also shown:

(1) **Solitary Mast Cell Tumour. (2) Two Cases of Necrobiosis Lipoidica, Non-diabetic, in Children.**—Dr. E. LIPMAN COHEN.

Congenital Epidermolysis Bullosa. — Dr. B. BENTLEY PHILLIPS.

Pityriasis Lichenoides et Varioliformis Chronica. —Dr. J. G. HOLMES.

Granuloma Annulare of Feet, with Features suggesting Sarcoid.—Dr. DENIS SHARVILL.

? Pityriasis Rubra Pilaris ? Tylosis Starting at Age 19.—Dr. P. J. FEENY and Dr. N. A. THORNE.

Lichen Myxœdematosus.—Dr. A. PORTER.

Angio-lupoid.—Dr. J. H. ALLISON (for Dr. F. RAY BETTLEY).

Hamartoma in a Boy of 10, Composed of Blood Vessel, Lymph Vessel, Fatty and Fibrous Tissue.—Dr. J. S. PEGUM.

Pachyonychia Congenita. A Case with an Associated Dystrophy of the Teeth.—Dr. E. WILSON JONES and Dr. H. J. WALLACE.

(1) **Chondrodermatitis Nodularis Helicis Chronica in a Housewife. (2) Prurigo Nodularis with Recovery.**—Dr. BEATRICE LEWIS.

Acute Lupus Erythematosus and Pulmonary Tuberculosis.—Dr. N. A. THORNE and Dr. A. GREENBERG (for Dr. R. H. S. HURST).

MR. J. S. CALNAN and Dr. B. ROSSATTI read a paper on **Some Observations on the Histopathology of Chondrodermatitis Nodularis Helicis Chronica.**

Meeting
December 18, 1958

Indeterminate Leprosy.—W. H. JOPLING, M.R.C.P., D.T.M.& H.

History.—Miss S. M., aged 24, an Indian from Kenya, came to England in May 1958. She has had no known contact with leprosy. During the past sixteen years she has noticed pale areas appearing on her skin and slowly becoming repigmented, and over the past four years she has developed sensory loss over the right hand followed by weakness and clawing of the outer 3 fingers. Recently she has noticed slight anæsthesia of her left hand. One month ago Mr. D. M. Brooks, of the Royal National Orthopædic Hospital, carried out a tendon grafting operation on the outer 3 fingers of her right hand.

On examination.—There are hypopigmented macules of various sizes on arms, thighs and left buttock, some showing slight sensory impairment, but there are no raised lesions or nodules. There is slight thickening of several peripheral nerves including the right ulnar nerve, and there is wasting of the intrinsic muscles of the right hand.

Skin smears and nasal scrapings are negative for acid-fast bacilli, and skin biopsy shows nothing more than very scanty infiltration by lymphocytes and mononuclear cells. The lepromin test is negative.

Comment.—This patient has irrefutable clinical signs of leprosy, yet there is nothing to support the diagnosis on histological and bacteriological examination. This type of leprosy is, therefore, quite distinct from the other types (lepromatous, borderline and tuberculoid) and the characteristic features are well shown by this patient, namely, skin lesions which are purely macular, peripheral nerve damage, a negative lepromin test, non-specific changes on skin biopsy and absence of acid-fast bacilli.

She commenced treatment with dapsone (DDS) four months ago, and the prognosis is good; the macules will re-pigment and there will be no further development of nerve damage. Had she been left untreated, the anæsthesia which has already appeared in the left hand might have been followed by muscle wasting and claw-hand deformity similar to that on the other hand. Further, as these patients are immunologically unstable they are liable to progress to one of the determinate types of leprosy, and this patient, with her negative lepromin test, might later have become borderline or lepromatous.

I would like to thank Sir George McRobert for permission to demonstrate this patient.

Dr. David Williams: Is nerve biopsy a feasible aid to diagnosis?

Dr. W. H. Jopling: Little work has been done on nerve sections in this type of leprosy, but I would expect an affected nerve such as the ulnar to show the presence of acid-fast bacilli and cellular infiltration. The important question is whether there are any suitable nerves which one could remove for sectioning. I am sure one would find acid-fast bacilli, in scanty numbers perhaps, in affected peripheral nerves.

Dr. E. J. Moynahan: Do these patients ever go on to develop the tuberculoid type?

Dr. Jopling: Yes, it is possible that some may do so. I think there would be a greater tendency for them to go to the lepromatous type, but there is no reason why a change in the host/parasite relationship should not bring about a tuberculoid change.

Dr. Moynahan: Have all these patients a negative lepromin test?

Dr. Jopling: It is possible to have a weakly positive test. A strongly positive test in patients with macules and nerve damage would indicate tuberculoid leprosy, and a skin section would show a tuberculoid type of cellular change.

Dr. M. Feiwel: Could Dr. Jopling tell us something about the new drugs which are being used in leprosy and the type of case in which they are most effective?

Dr. Jopling: I heard a great deal about new drugs when I was in Tokyo last month at the 7th International Leprosy Congress, and I would like to mention the two which I consider most important. The first is the diphenyl thiourea compound Ciba 1906. It is proving as effective as the sulphone group and has the advantage of being non-toxic. This is an important point, for the toxic effects of sulphone can be troublesome. It is, however, more expensive. Some patients have been treated with this compound for as long as three to four years, and that is a critical time for the possible development of resistance on the part of the leprosy bacilli. Dr. T. F. Davey in Nigeria has found resistance developing in a few instances at about the 40th month of treatment, but we are not yet in a position to say if this is likely to be a universal finding. Ciba 1906 can be prescribed on Form E.C.10.

The other big development in therapy is the production by I.C.I. of a derivative of ethyl mercaptan called ETIP. It has to be administered by inunction, and is still in the research stage. The most striking observation has been the rapid fall in the bacterial index of lepromatous cases within six to twelve weeks, and such a rapid action would suggest that its antibacterial action is entirely different from that of all other anti-leprosy drugs and is probably bactericidal. The chief disadvantage is that the leprosy bacilli appear to develop resistance after about three months, and therefore the drug can be used, on its own, for only a limited period of time. Work has yet to be done on combined treatment with other drugs. I feel sure that further research on derivatives of ethyl mercaptan will lead to still more sensational results.

Unusually Widespread Tinea Corporis.—C. M. RIDLEY, M.R.C.P.

S. M., male, aged 33. Sales clerk.

History.—Scaliness and redness of previously normal skin for about ten years. Deformity of the nails, worse recently, for about three years. General health good. Abroad only in Europe. Wife is unaffected.

Family history.—No similar skin trouble. No dryness of the skin.

Clinical findings.—Almost universal erythema with scaling (some fine and some ichthyosiform); face, neck, central back and axillæ and antecubital fossæ largely spared; scalp appears clear. No suggestion of an active edge at any site; at the axillæ and on the back, however, there are well-defined borders. Soles and palms red with annular and branny scaling. Many toe and finger nails heaped up and discoloured.

Investigations.—E.S.R. 3 mm. in one hour (Westergren). Hb 100%, W.B.C. 6,000, normal differential count.

Biopsy.—(1) From right chest: Small foci of intercellular œdema in epidermis and PAS-positive fungal elements present in the keratotic layer. (2) From right axilla: No histological abnormality. PAS-negative.

Scrapings.—(1) Toe nail, finger nail, palm and sole: much fungus present. (2) Scaly areas on face, chest, thigh, arm: much fungus present. (3) Apparently normal skin of centre of back: no fungus seen. (4) Apparently normal skin of axillæ: fungus present (on two occasions).

Cultures.—Nails: so far negative. Skin (2 sites): *Epidermophyton floccosum.*

Comment.—This patient is unusual in that the lesions are almost universal. It is of interest too that fungus has been found on apparently normal skin. That this finding results from a chance scattering of fungus on the surface is suggested by the negative PAS stain on a section from the area. Treatment promises to be difficult; griseofulvin is to be given.

Dr. L. Forman: I have under treatment a similar case who presented as an exfoliative dermatitis. This developed after penicillin therapy for boils. Scrapings from the thigh showed fungus to be present. When the erythroderma subsided, the skin remained generally scaly. At any site, scrapings showed massive invasion of fungus, shown by Miss B. M. Partridge at the Institute of Dermatology to be *Epidermophyton floccosum*. Prolonged treatment with local fungicides has been completely unsuccessful.

Dr. E. J. Moynahan: Several cases of generalized fungus infection have been described following cortisone treatment. I do not think this is particularly unusual. With regard to the distribution of different species of fungi on the skin I would say that *Epidermophyton floccosum* and the common trichophytes tend to avoid areas where sebaceous secretion is present. Nickerson has shown that certain fungi prefer to live on certain parts of the skin. This patient must be relatively unusual only in his reduced resistance to fungus infection.

I have had a patient who had such a reduced resistance to *Trichophyton rubrum* that he only needed to go to a slightly warmer district such as the South of France for the lesions to spread rapidly all over the exposed skin of face and hands. There are some individuals who show this markedly reduced resistance to fungus infection and it seems that patients who have had a great deal of ACTH and cortisone may be rendered more liable to widespread fungus infection.

Dr. G. A. Beck: I agree that this is a beautiful case but I would think that it is not quite so rare as has been suggested.

I have seen two or three such widespread cases. One, a very old man at St. John's Hospital, had an extensive rash on his body which, when we scraped it, grew *T. rubrum*. We also got *T. rubrum* from most of the other more usual sites. It cleared clinically fairly readily from his trunk but he still showed rubrum in scrapings from the apparently normal skin of his body.

Another is a war pensioner invalided out with universal eczema. When I saw him ten years later he still had widespread eczematous lesions on the lower limbs and lower part of his trunk. On scraping I found fungus, both in the clinically active eczematous areas, and in areas I regarded as normal allowing for the fact that he had had such extensive eczema for so long a time.

Dr. David Williams: I do not know whether I should say anything about griseofulvin. It is a very remarkable drug, although it does not seem to touch moniliasis, actinomycosis, blastomycosis or versicolor.

We have so far only treated 23 cases. Of 3 cases of ringworm of the scalp, 1 was quite readily and easily cured and the other 2 look as if they are going the same way; ordinary ringworm on the body disappears in two to three weeks. Infected nails appear to be growing out normally, but assessment of this is a long-term business. As to toxic effects, they have been so far negligible. I would expect this case to respond very well.

The President: We have had 2 patients develop a toxic erythema after this drug, one with sickness; 10 other cases had no ill-effects.

The following cases were also shown:

Lichenoid Reticulosis of the Nape.—Dr. W. N. GOLDSMITH.

Infantile Eczema Treated by Psychotherapy.—Dr. H. JULIE ALTSCHULOVA (for Dr. P. J. HARE).

Lifelong Besnier's Prurigo Treated by Weekly Psychotherapy.—Dr. H. JULIE ALTSCHULOVA (for Dr. W. N. GOLDSMITH).

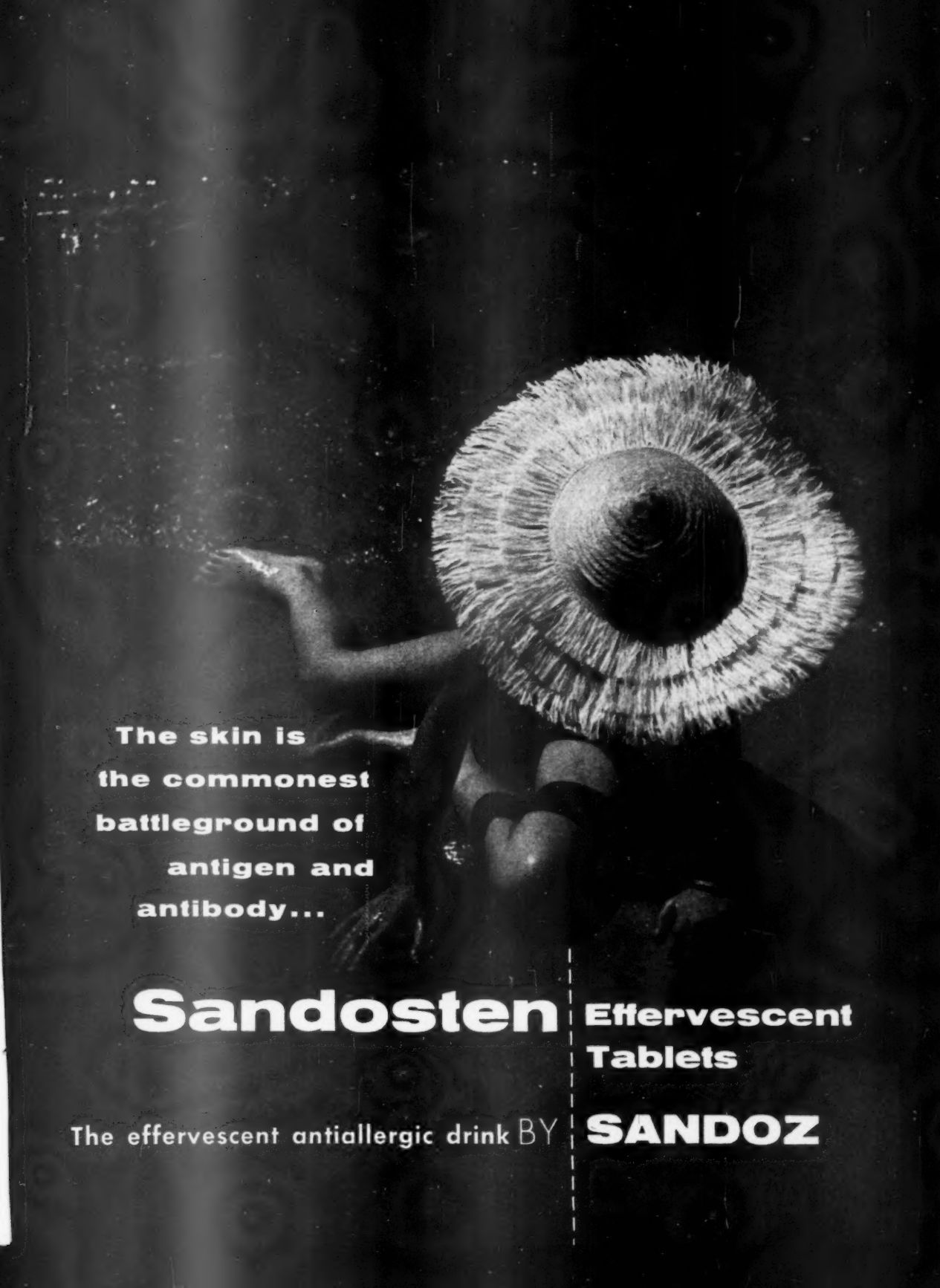
(1) **Hypodermite Nodulaire wtih Uveitis. ? Periarteritis Nodosa.** (2) **Hypodermite Nodulaire. ? Bazin's Disease in a Man.**—Dr. P. J. HARE.

Intrapapillary Elastoma Perforans (Miescher).—Dr. HAROLD WILSON.

Multiple Angiomata.—Dr. E. CRONIN (for Dr. H. J. WALLACE).

Lichen Amyloidosus.—Dr. D. C. G. BETT (for Dr. LOUIS FORMAN).

Scarring Nail Dystrophy.—Dr. E. WILSON JONES.


The skin is
the commonest
battleground of
antigen and
antibody...
Sandosten
Effervescent
Tablets
The effervescent antiallergic drink BY
SANDOZ

Relief without risk!

CALPOL TABLETS

a safe, non-irritant, low cost analgesic

CALPOL

* A **NON-SALICYLATE** analgesic and antipyretic
* No adverse cardiac effects
* Rapidly absorbed and quick acting
* Does not cause occult bleeding. Non-constipating
* Suitable for children
* May be given to dyspeptics and peptic ulcer patients without any undesirable side effects
* For occasional or prolonged use

INDICATIONS For use whenever a safe analgesic or antipyretic is required. For relief of rheumatic pain, dysmenorrhoea, headaches, coryza, influenzal states, tonsillitis and all other pyrexial conditions.

DOSE **Adults:** 1 or 2 Tablets repeated after 3-4 hours if necessary.
Children:
2-6 years of age ¼-½ Tablet.
7-12 years of age ½-1 Tablet.

FORMULA Each tablet contains 0.5 gm. Paracetamol.

TRADE PRICES 50 pack 3/11 exempt P.T.
500 pack 31/- exempt P.T.

CALPOL

CALMIC LIMITED · CREWE · CHESHIRE · TELEPHONE CREWE 3251-7
LONDON: 2 Mansfield Street, W.1. *LANgham 8038/9*

Section of Comparative Medicine

President—F. O. MacCallum, M.D.

Meeting
December 17, 1958

Spontaneous Gastric Dilatation in Man

By D. E. Bolt, F.R.C.S.
Isleworth, Middlesex

Spontaneous gastric dilatation in man is a rare condition and opportunities of studying it consequently few. The dilatation is mainly gaseous but the source of the gas and the reason that the stomach fails to expel it are obscure. Certain features of ætiology and pathology resemble those of bloat in the ruminants and invite comparison between the disorder in man and animal.

A brief account of a personal case suggests the characteristic picture in man.

At 12.30 a.m. on February 5, 1958, a man of 37 was admitted to hospital from a home for mental defectives where he had lived since childhood. In normal health until 11 p.m. on February 4, he was then seized with severe abdominal pain and retched repeatedly without vomiting. He had a grossly distended abdomen with mottled cyanosed skin and with an absolute wooden rigidity more pronounced than is usual in patients with perforation of a peptic ulcer. Despite a normal circulation and blood pressure in his arms, his legs were cold, mottled and pulseless and appeared anæsthetic and paralysed. A Ryle's tube produced only a little brown fluid. In the belief that spontaneous rupture of the stomach had occurred, laparotomy was performed. The tightly stretched peritoneum was incised with great care and a loud, prolonged escape of gas followed, with disappearance of the abdominal distension. On inspecting the abdomen it was clear that the final incision had opened the stomach, tightly pressed against the abdominal wall, and the escaped gas had been intragastric but there had been no escape of froth or fluid and the peritoneum was unsoiled. No other abdominal lesion or apparent obstruction to either orifice of the stomach was found; the gastric incision was sutured and the abdomen closed. The patient died about two hours after the operation without regaining consciousness but with recurrence of his abdominal distension. The circulation to his legs, which had returned to normal after operation, had again been occluded by the time he died. The post-mortem showed no mechanical obstruction at cardia or pylorus, but the stomach and duodenum contained a considerable quantity of raw peas. A smell resembling stale alcohol or vinegar was most pronounced at post-mortem, as it has been before death. The cause of death was extensive bilateral pulmonary collapse associated with great elevation of the diaphragm.

Iti s possible that this patient might have been saved by the effective use of a large stomach tube, although Hillemand *et al.* (1947) report rupture of the stomach occurring with one in place, or by a temporary gastrostomy, although this also failed in a case reported by Leger and Mäes (1947).

In human cases the usual cause of death is rupture of the stomach, Rejthar (1952) finding about 30 cases in the literature. The mentally retarded appear to be particularly liable to it. The preceding meal is usually heavy and contains mainly vegetable; peas, raisins, plums and sauerkraut are typical examples. Sodium bicarbonate taken medicinally (Millar *et al.*, 1957) or used in excessive amounts in a cake (Chipail *et al.*, 1948) appears to have provoked attacks, while several records suggest that copious water drinking soon after a meal contributed to disaster. Ladkin and Davies (1948) reported spontaneous rupture of the stomach after a large meal of African sweet potatoes, a smell of vinegar being noticed clinically and at post-mortem. They found that organisms from the stomach hydrolysed the sugars in sweet potatoes with liberal gas formation but such investigations on post-mortem material are of doubtful significance.

In man, therefore, this condition is one of very gross gaseous distension of the stomach, occurring in the absence of organic obstruction and commonly following the excessive ingestion of vegetables or of substances containing readily liberated gases. It is clearly distinct from the commoner acute dilatation of the stomach complicating abdominal surgery, which is painless, is accompanied by profuse vomiting and causes death by fluid and electrolyte loss, not by rupture of the stomach. Spontaneous gastric dilatation resembles bloat in various ways. The types of food most commonly producing the two conditions have similar possibilities of fermentation, while in both there is an added risk if water is taken soon after the meal. The nature of the gas has never been determined in man but in several reported cases it was almost certainly carbon dioxide. There is no evidence that bloat in ruminants is necessarily associated with particularly greedy feeding (Johns, 1956), but it is also true that the previous meal has not invariably been excessive in human cases. Certainly, in both species very high intragastric pressures may be produced—sufficient to overcome normal blood pressure in 2 human cases—while Boda

et al. (1956) recorded an intraruminal pressure of 86 mm.Hg in a cow with bloat.

The fundamental functional difference between the non-glandular rumen and reticulum of animals and the glandular stomach of man might be felt to exclude any close comparison between the condition in the two species, but if the source of the gas in ruminants is bacterial fermentation of sugars with gas production (Belscher, 1950) it is tempting to accept the view suggested by Ladkin and Davies (1948) to explain their case which followed a meal of African sweet potatoes. In general, however, bacterial fermentation can hardly be a factor in man, except perhaps in the presence of achlorhydria, but fermentation by enzymes or yeasts might occur within a large vegetable mass, protected by its bulk from the action of hydrochloric acid, even in the human stomach. The very high pressures and the alcoholic smell are in keeping with a fermentation process occurring in a closed space, as is the rapid recurrence of distension in an anæsthetized patient in whom air swallowing could hardly occur. This raises the question of why the human stomach or the animal rumen should behave as a closed space. In both cases distal passage of gas may be prevented by the bulk of a heavy vegetable meal, although this did not appear to be true in the case described above, but in man, once distension is established, gastric peristalsis will cease and the pylorus probably go into spasm. In a series of experiments on the human stomach at post-mortem, it was found that if the pylorus was ligatured and the stomach inflated through a needle connected to a hand pump and a manometer, gas escaped up the œsophagus as soon as the pressure in the stomach exceeded 40 mm.Hg. If, however, only a small incision was made in the abdominal wall, so that the relationship between stomach and parietes was not disturbed, and the intragastric pressure was raised rapidly, in several cases pressures of 240 mm.Hg (the limit of the manometer in use) were supported without leak up the œsophagus. Unfortunately, any attempt to enlarge the incision or to explore with the hand to discover the exact mechanism responsible led to immediate emptying of the stomach through the œsophagus, but it was thought that when the gastric fundus became distended with gas at a high pressure it might well displace the abdominal œsophagus and kink it against the right crus of the diaphragm, producing an occlusion increasingly secure as the pressure rose and very difficult to traverse with a stomach tube.

This does not, of course, explain the failure of the patient to expel the gas before these high pressures are reached. It is probable that in ruminants free gas bloat is preceded by frothy bloat (Fincher, 1956; Johns, 1956), the froth being difficult to eructate and producing distension of a degree which prevents satisfactory contraction of the rumen in order to expel free gas when it develops. No evidence can be found that such a stage occurs in humans and no froth emerged from the stomach described above when incised at operation, but the stage of froth may well have been passed by the time the reported cases came under treatment. It is clearly probable, however, that the mechanism producing these remarkable degrees of gastric distension is fundamentally the same in man and animals and that the human condition may be clarified incidentally as understanding of the mechanism of bloat in the ruminants increases. It may be that only his gastric acidity and relatively modest vegetable diet prevent man from suffering commonly from bloat.

My thanks are due to Mr. W. J. Ferguson, under whose care the case described was admitted, for permission to report it; to Dr. Donald Teare for performing the post-mortem; and to Dr. A. Knudson for his valuable advice and suggestions.

REFERENCES

Belscher, H. G. (1950) Sheep Management and Diseases. Sydney; p. 524.
Boda, J. M., Cupps, P. T., Colvin, H., and Cole, H. H. (1956) *J. Amer. vet. med. Ass.*, **128**, 532.
Chipail, G. G., Wassermann, L., and Lazarovici, I. (1948) *Arch. Mal. Appar. dig.*, **37**, 479.
Fincher, M. G. (1956) Diseases of Cattle. Evanston, Ill., p. 190.
Hillemand, P., Leger, L., and Renault, A. (1947) *Bull. Soc. méd. Hôp. Paris*, **63**, 607.
Johns, A. T. (1956) *Vet. Rev. Annot.*, **2**, 107.
Ladkin, R. G., and Davies, J. N. P. (1948) *Brit. med. J.*, i, 644.
Leger, L., and Mäes, J. (1947) *J. Chir., Paris*, **63**, 35.
Millar, T. M., *et al.* (1957) *Brit. J. Surg.*, **44**, 513.
Rejthar, R. (1952) *Brit. med. J.*, ii, 324.

Physiological Effects of Distension of the Rumen and Œsophagus in Ruminants

By R. N. B. Kay, M.A., Ph.D., and A. T. Phillipson, Ph.D., M.R.C.V.S.
Bucksburn, Aberdeenshire

Bloat is a fairly common disease of cattle and sheep, characterized by gross distension of the rumen. It is now generally accepted that the distension is due to foaming of the digesta in the rumen, which involves both plant and animal factors, and that the animal is unable to eliminate the foam by belching. This paper is not concerned with the causes of foaming but with the physiological effects of rumen distension. For this it is necessary to consider not only the rumen but also the œsophagus and other parts of the stomach which may become distended.

Rumen distension has three main effects: it causes changes in salivation, changes in the eructation reflex and changes in respiration and blood pressure. We will first discuss salivation in some detail as we have recently studied the problem (Kay and Phillipson, 1957).

It has been suggested by Johns (1958) that an increased flow of saliva could be of considerable importance in the development of bloat. Not only does the mucoprotein of mixed ruminant saliva form a strong and stable foam but the saliva also contains about 100 mM./l. of carbon dioxide, much of which will be released to add to the foam when the pH of the saliva is reduced to that of the rumen contents. The volume of gas required to raise the rumen pressure by 10-mm.Hg steps decreases greatly as the rumen pressure is raised (Table I), so that once slight bloat has developed the production of only a small additional volume of rumen gas could rapidly worsen the condition.

TABLE I.—VOLUMES OF GAS REQUIRED TO RAISE THE RUMEN PRESSURE OF A SHEEP BY 10-MM.HG STEPS

Increase in rumen pressure (mm.Hg)	Volume of CO_2 required (l.)	Volume of N_2 required (l.)
0–10	5·0	5·3
10–20	3·6	3·5
20–30	2·6	2·1
30–40	1·1	0·8

Phillipson and Reid (1958) found that inflation of the rumen of anæsthetized sheep and calves to a moderate pressure often increases the flow of parotid saliva and that of the residual saliva dripping from the mouth. Inflation of the rumen to higher pressures inhibits this effect. These responses varied from one preparation to another. We have pursued the problem further in order to define the excitatory and inhibitory components of the response and to find which salivary glands are affected.

Sheep and calves under chloralose anæsthesia were used. In the first experiments the œsophagus was tied in the neck and the rumen was inflated through a cannula. Inflation of the rumen to pressures below about 20 mm.Hg increased the flows of parotid and residual saliva up to tenfold, but had little effect on the scant submaxillary and sublingual secretions. Further increases in pressure progressively inhibited the responses, although they returned when the pressure was reduced again. Approximately equal quantities of parotid and residual saliva were secreted. The latter consisted of two components, a fluid saliva secreted by the serous inferior molar glands, and an extremely mucous saliva secreted by the small mucous glands that lie beneath the epithelium of the cheeks, palate and pharynx.

It is known that parotid secretion can be increased in ruminants by distending the œsophagus, so the œsophagus and rumen were inflated independently after tying the œsophagus just above the cardia. Inflation of the œsophagus alone stimulated parotid secretion; inflation of the rumen alone inhibited this response. Similar responses were obtained when the œsophagus was distended with air, CO_2, N_2, O_2, 0·9% saline solution, rumen liquor or balloons, so that the œsophageal receptors appear to response to the mechanical effects of distension rather than to any chemical stimulus. The use of balloons also showed that greater responses were obtained from the thoracic than from the cervical œsophagus.

Balloons were also used to distend various parts of the rumen. When these were inflated in the dorsal or ventral sacs of the rumen they usually but not always inhibited parotid secretion, but stretch of the reticulo-rumen fold was always stimulatory (Comline and Titchen, 1957). Section of the cervical vagus nerve abolished excitatory responses from the œsophagus and rumen, while section of the vagus at the level of the diaphragm abolished a large part of the inhibitory effect of rumen distension.

Inflation of the abomasum had a slight inhibitory effect on parotid secretion in some preparations but not in others. This is similar to the weakly inhibitory effect of abomasal distension on eructation (Weiss, 1953) and contrasts with the strongly inhibitory effect on reticulum contractions (Phillipson, 1939).

Eructation in ruminants takes place in three stages. Free rumen gas is moved to the antrum of the cardia by a contraction of the rumen, the cardia relaxes and admits gas into the œsophagus and the gas is eliminated by relaxation of the cranial œsophageal sphincter and contraction of the œsophagus (Dougherty and Meredith, 1955; Dougherty and Habel, 1955). It is generally agreed that eructation is stimulated reflexly by distension of the rumen with gas. Weiss (1953) has suggested that the receptors for this lie in the posterior dorsal sac of the rumen, but Dougherty and his colleagues in Cornell have evidence that the region of the cardia is more important. Dougherty *et al.* (1958) stimulated eructation in decerebrate sheep by inflation of the rumen through a cannula. When the rumen contained digesta or water this response was inhibited by turning the preparation on to its back, but this did not inhibit when the rumen was empty. The inhibitory effect appeared to be due to submergence of the cardia under fluid. Eructation could also be stimulated or inhibited by inflating or flooding a small pouch made from the anterior part of the rumen and including the cardia. In earlier cinefluorographic studies (Dougherty and Meredith, 1955; Dougherty and Habel, 1955) the Cornell team had shown that the cranial œso-

phageal sphincter will relax when the œsophagus becomes distended with gas as in normal eructation, but not when it is distended with water.

Stomach movements and eructation continue during the early stages of bloat (Johns *et al.*, 1957). Dougherty *et al.* (1958) suggest that although eructation is attempted, its efficiency may be reduced, presumably because the cardia is covered by digesta and the œsophagus is filled with foam, and that this inefficiency will hasten the development of bloat.

The third effect of rumen distension is on respiration and blood pressure. The importance of respiratory changes is indicated in one of the few reports that describe the sequence of events in a fatal case of bloat; this concerned a cow that had eaten 29 lb. of fresh alfalfa tops (Boda *et al.*, 1956). An hour after the meal the animal was severely bloated and its respiration was laboured. Shortly afterwards it fell on one side and stopped breathing although its pulse continued for another four minutes. Inhibition of respiration was also demonstrated in experimental studies at Cornell on conscious sheep (Dougherty *et al.*, 1955). Brief periods of inflation of the rumen to pressures of 40–80 mm.Hg slowed or stopped respiration, with consequent reduction in oxygen consumption and arterial oxygen levels. Sharp increases and fluctuations of blood pressure also occurred. Similar changes in respiration and blood pressure have been found in anæsthetized sheep (Phillipson, 1958).

In experiments on anæsthetized sheep we have found that during the early stages of rumen inflation there is a small stepwise increase of blood pressure with rumen pressure, but eventually apnœa and violent fluctuations in blood pressure occur. The changes in blood pressure may be due to some extent to the obstruction of blood flow through the inferior vena cava, for during rumen inflation we have found the pressure in the abdominal vena cava to be little less than rumen pressure.

Speaking generally, it seems that two groups of responses are excited by distension of the rumen. Pressures of below 20–40 mm.Hg, corresponding to mild bloat, may stimulate salivary secretion as a result of œsophageal distension, stimulate eructation and cause slight increases in blood pressure. Higher pressures, corresponding to severe bloat, inhibit salivation and eructation and eventually inhibit respiration. Although little work has been done so far on the respiratory and pressor effects of rumen distension enough is known to suggest that such effects could account for the terminal stages of bloat and for the death of the animal. Hence there is no need at present to postulate systemic poisoning by plant saponins or other toxic substances. The fact that bloat can be relieved by the timely administration of antifoaming agents also argues strongly against the involvement of any toxic factor.

REFERENCES

Boda, J. M., Cupps, P. T., Colvin, H., and Cole, H. H. (1956) *J. Amer. vet. med. Ass.*, **128,** 532.

Comline, R. S., and Titchen, D. A. (1957) *J. Physiol.*, **139,** 24P.

Dougherty, R. W., and Habel, R. E. (1955) *Cornell Vet.*, **45,** 459.

——, ——, and Bond, H. E. (1958) *Amer. J. vet. Res.*, **19,** 115.

——, and Meredith, C. D. (1955) *Amer. J. vet. Res.*, **16,** 96.

——, ——, and Barrett, R. B. (1955) *Amer. J. vet. Res.*, **16,** 79.

Johns, A. T. (1958) *Vet. Rev. Annot.*, **4,** 17.

——, Mangan, J. L., and Reid, C. S. W. (1957) *N.Z. vet. J.*, **5,** 115.

Kay, R. N. B., and Phillipson, A. T. (1957) *J. Physiol.*, **139,** 7P.

Phillipson, A. T. (1939) *Quart. J. exp. Physiol.*, **29,** 395.

—— (1958) Control of Diseases in Cattle and Sheep at Pasture. EPA/OEEC publ. Project 204, p. 50.

——, and Reid, C. S. W. (1958) *Nature, Lond.*, **181,** 1722.

Weiss, K. E. (1953) *Onderstepoort J. vet. Res.*, **26,** 251.

Bloat in Cattle

Aspects of Research Work at Plant Chemistry Division, D.S.I.R., Palmerston North, New Zealand

By J. L. Mangan, M.Sc., Ph.D.

Cambridge

Bloat is a disorder in ruminants common in all parts of the world where the grazing of legumes is practised. In New Zealand where the legume is depended upon to supply the total nitrogen required by the pasture, and where the pasture often becomes clover-dominant, it is particularly widespread. One of the main difficulties in research with bloat has been the sporadic nature of its occurrence. Johns (1954) initiated the use of identical twin cows chosen for their susceptibility or resistance to bloat and by stall feeding these animals on fresh red clover, bloat could be regularly produced in the spring and autumn. Preliminary studies indicated that the ailment was caused by foaming of the rumen ingesta whereby fermentation gases were retained as a stable foam which could not be eliminated by the belching mechanism. A number of antifoaming agents were found to prevent bloat or to relieve the condition after the animal was bloated. Rumen movements and the eructation mechanism were not inhibited during the early stages of bloat.

The "tympanograph", an adaptation of the corrugated rubber tube stethograph, was devel-

oped by Reid (1957) to measure changes in abdominal girth of stall-fed animals. Using this instrument, which recorded on a kymograph, accurate measurement of the rate and degree of bloating and the rate of deflation of the animals could be made. A large number of substances (Reid and Johns, 1957) were tested on identical twin cows both as a treatment for bloated cows and as a prophylactic. The vegetable oils, whale oil, emulsified tallow, liquid paraffin, &c., were found to be rapidly effective, badly bloated animals being deflated in about 30 min. Avlinox, a polyethylene glycol derivative of ricinoleic acid, was similarly effective. Silicones and several detergents were not reliable while a variety of irritants and antihistaminics were ineffective. As a result of this work (Reid, 1958), the spraying of bloat-producing pasture with emulsified peanut oil or tallow is now standard farming practice in New Zealand and parts of Australia.

If the foam theory of bloat is to be accepted, it is important to know if the ruminant can belch foam. Dougherty and Habel (1955) and Dougherty and Meredith (1955) in the U.S.A. had shown that three sphincters in the œsophagus were involved in belching, the sphincter at the cranial end being most efficient. Liquid was found to inhibit the opening of this sphincter. While at Plant Chemistry Division, Palmerston North, Dougherty (1955, unpublished) extended this work to foams. Using his isolated reticular pouch preparation in decerebrate sheep it was found that the cranial sphincter would not open to foams and considerable pressure could be built up in the pouch. This sphincter opened quite readily to free gas.

Foaming Properties

Adopting the foam theory, the first step from a chemical point of view is to identify the causative foaming agent. For an animal feeding on a legume, there are three obvious foaming agents entering the rumen:

(1) The plant saponins.
(3) The leaf-cytoplasmic protein.
(3) The mucoprotein secreted in the saliva.

A fourth type of foaming agent, the extracellular bacterial polysaccharide, has been suggested by Hungate *et al.* (1955) as the cause of "feed-lot" bloat in the U.S.A.

It is rather difficult to decide what properties of foams are of significance in any particular problem, and in the present work measurements were made of foam expansion, dynamic foam stability and foam strength (Mangan, 1957). Of these, foam strength was found to be most useful. The three systems mentioned above were all found to be sensitive to pH changes. The saponins from lucerne and red clover showed maximum foam strength at pH 4·5 to 5·0 and outside this range, although foams were formed, they had reduced mechanical strength.

Leaf cytoplasmic protein isolated from red clover, at a relatively low concentration of 10 mg.N/100 ml. and in the presence of electrolytes, produced extremely stable and mechanically strong foams with a maximum in the range pH 5·4 to 6·0. When no salt was present, no foam was produced, but there was a rapid and linear increase in foam strength with increase of salt concentration up to 0·33 M.

Salivary mucoprotein is an extremely efficient foaming agent even at the low concentration of 5 mg.N/100 ml. but owing to the heterogeneous nature of the salivary protein, the response to pH changes is not consistent. In all cases, the greatest foam strength occurred above pH 7·5, but the saliva from some cows showed a secondary peak at about pH 6·5. Lyttleton (1957, unpublished), in electrophoretic studies, has shown that there are two major proteins in bovine saliva, one of which is a normal protein and the other a mucoprotein. The ratios of the two components differ and work on identical twin cows indicates that the difference may be inherited. Further work is required to show if this is a factor in the susceptibility to bloat.

Examination of crude rumen liquor (Mangan, 1959) showed that there was a naturally occurring antifoaming agent present which was shown indirectly to be chloroplast material from the leaf. High speed centrifuging of crude rumen liquor gave a solution which normally produced a fine bubble foam of greatly increased foam strength. Clear rumen liquor obtained from a cow after one hour's feeding on red clover showed a response to pH changes very similar to that obtained with cytoplasmic protein, the optimum pH being between 5·4 and 5·7.

Contrary to expectation, it was found that with cows feeding on clover, large quantities of soluble protein were released into the rumen fluid. After two hours' feeding the soluble protein level normally rose to 20–25 mg.N/100 ml. On cessation of feeding, the soluble protein level dropped rapidly. This concentration of soluble protein, at the salt concentration found in the rumen, is sufficient to produce a very strong and stable foam.

In a study of pH changes in the rumen fluid, Reid (1956, unpublished) found that for a cow to commence bloating on red clover, the pH must fall to 6·3 and as the condition develops, the pH drop normally continues occasionally to as low as 5·7. Of the systems studied, the foaming properties of cytoplasmic protein would suggest that it is the active foaming agent responsible for bloat, but salivary protein may make a contribution.

Saliva

Colin (1886), Markoff (1913) and more recently Balch (1954) have shown that the cow secretes about 50–60 litres of saliva per day, most of which is produced while the animal is eating. This normally functions as a bicarbonate phosphate buffered medium for microbial fermentation in the rumen and reticulum. In relation to bloat it would tend to prevent bloat by opposing a drop in pH to the critical value. There are two other factors concerning saliva, however, which would contribute towards bloat.

(1) Under bloating conditions, the pH of the rumen fluid is about 6·0. Saliva secreted at pH 8·5 on entering the rumen will then evolve carbon dioxide by decomposition of bicarbonate. Each litre of saliva will liberate approximately 2 litres of carbon dioxide or a total of about 100 litres per day. This may be an important factor when the animal is fed on bloat-producing clover after having been deprived of food for some time.

(2) The submaxillary mucoprotein which has powerful foaming properties is secreted in large amounts while the animal is eating.

It should be pointed out that much of the earlier work relating saliva to bloat has not taken into account the fact that there are at least three distinct secretions, the parotid, submaxillary and residual salivas, the latter being a mixture composed partly of sublingual. These secretions have quite different chemical properties and react differently to stimuli.

Phillipson and Reid (1958) at Plant Chemistry Division showed that the rate of flow of saliva in some sheep and calves responded markedly to an increase in rumen pressure. A relatively low pressure of 8–20 mm. Hg often produced a greatly enhanced flow of parotid, submaxillary and residual salivas. Occasionally, only the submaxillary and residual secretions responded. Further increases in pressure after stimulation caused an inhibition of secretion.

The chemical composition of these salivas and the effect of rumen pressure stimulation was examined by Mangan and Phillipson (1959, in preparation) and a typical example is shown in Table I. It should be noted that the composition of the parotid and residual secretion is not markedly changed despite the greatly increased rate of flow but with the submaxillary saliva the concentration of mucoprotein is increased fivefold. It seems probable that if a reactive animal bloats mildly, the increase in salivary flow due to pressure in the rumen could aggravate the condition by an increased gas evolution from bicarbonate and supply of further foaming agent.

Penicillin

Work on the control of bloat at Plant Chemistry Division has been directed mainly towards the use of antifoaming agents to suppress foam in the rumen, but Barrentine *et al.* (1956) in the U.S.A. first used antibiotics, mainly penicillin, to prevent bloat by depressing gas production.

Field trials at Palmerston North (Johns, 1958) showed that 200,000 units of penicillin every second day did not eliminate bloat, but that the incidence and severity were greatly restricted.

Using identical twin cows, Johns, Mangan and Bailey (1959, in preparation) showed that penicillin greatly altered chemical reactions in the rumen. In penicillin-treated animals, nutrients released from the clover rapidly accumulated in the rumen. Soluble protein and free amino acids built up to much higher concentrations than in the control animals whereas ammonia production was curtailed. Free sugars which normally are not found in the rumen appeared in the rumen liquid in appreciable amounts, and volatile fatty acids were not produced normally; instead lactate accumulated in abnormal concentrations. Penicillin treatment reduced the foaming properties of the crude rumen liquor almost to nil, but on the cleared liquor the position was reversed and the penicillin-treated sample had remarkably powerful foaming properties. This behaviour is probably due to the presence of large quantities of soluble protein and to the chloroplasts not having been degraded by microbial action and thus exerting their full antifoaming action.

After repeated treatment with penicillin, it was found that resistant strains of rumen organisms appeared and the above effects disappeared. Again, after a period of no treatment, the "typical" behaviour reappeared.

Carbohydrates

Bailey and Oxford (1958) have studied the production of dextran, a glucopolysaccharide, by strains of *Streptococcus bovis* isolated from the rumen. *In vitro* large quantities of dextran were produced when sucrose was the source of carbo-

Table I.—Composition of Normal and Rumen-Pressure-Stimulated Salivas

Sample	Nitrogen (mg.N/100 ml.)			Anions (mEq./litre)			Cations (mEq./litre)		
	Total	Urea	Protein	HCO_3^-	HPO_4^-	Cl^-	Na^+	K^+	Ca^{++}
Parotid	14·6	11·5	1·5	113·8	22·0	22·1	122	12·2	2·7
Parotid*	14·8	12·5	1·0	116·3	27·0	9·2	122	13·7	3·5
Submaxillary	29·2	9·0	19·5	19·6	1·2	22·0	12·9	14·2	10·1
Submaxillary*	116·8	13·1	95·3	17·2	2·6	49·2	15·8	14·3	7·6
Residual	20·4	10·1	9·8	94·2	19·2	33·0	103	18·2	3·8
Residual*	22·8	9·3	12·1	104·2	17·0	17·5	142	19·4	3·2

*Rumen-pressure-stimulated.

hydrate and only in the presence of carbon dioxide. Bailey (1958*a*) has found that red clover contains about 3–4% sucrose on dry weight basis, but examination of rumen fluid (Bailey, 1959, in press) from bloating cows showed only traces of extracellular polysaccharide. Other organisms presumably compete successfully for sucrose.

Bailey (1958*b*) has shown starch to be a major component of the carbohydrates present in red clover under suitable weather conditions. Bailey (1958*c*) and Oxford (1958) found that *Epidinium ecaudatum*, an oligotrich protozoa which is present in large numbers in the rumen of clover-fed cows, will rapidly ingest red clover starch grains, but not the larger grains from other plants, e.g. potato starch. The indications are that this organism may be of importance in carbohydrate metabolism in relation to bloat.

REFERENCES

BAILEY, R. W. (1958*a*) *J. Sci. Fd. Agric.*, **9**, 748.
—— (1958*b*) *J. Sci. Fd. Agric.*, **9**, 743.
—— (1958*c*) *N.Z. J. Agric. Res.*, **1**, 825.
BAILEY, R. W., and OXFORD, A. E. (1958) *J. gen. Microbiol.*, **19**, 130.
BALCH, C. (1954) *Rep. nat. Inst. Dairy., Reading*, p. 44.
BARRENTINE, B. F., SHAWVER, C. B., and WILLIAMS, L. W. (1956) *J. Anim. Sci.*, **15**, 440.
COLIN, G. E. (1886) Traité de Physiologie-comparée des Animaux. Paris.
DOUGHERTY, R. W., and HABEL, R. E. (1955) *Cornell Vet.*, **45**, 459.
——, and MEREDITH, C. D. (1955) *Amer. J. vet. Res.*, **16**, 96.
HUNGATE, R. E., FLETCHER, D. W., DOUGHERTY, R. W., and BARRENTINE, B. F. (1955) *Appl. Microbiol.*, **3**, 161.
JOHNS, A. T. (1954) *N.Z. J. Sci. Tech.*, **36A**, 289.
—— (1958) *Vet. Rev. Annot.*, **4**, 17.
MANGAN, J. L. (1957) *N.Z. J. Agric. Res.*, **1**, 140.
—— (1959) *N.Z.J. Agric. Res.*, **2**, 47.
MARKOFF, J. (1913) *Biochem. Z.*, **57**, 1.
OXFORD, A. E. (1958) *N.Z. J. Agric. Res.*, **1**, 809.
PHILLIPSON, A. T., and REID, C. S. W. (1958) *Nature, Lond.*, **181**, 1722.
REID, C. S. W. (1957) *N.Z. J. Sci. Tech.*, **38A**, 853.
—— (1958) *N.Z. J. Agric. Res.*, **1**, 349.
——, and JOHNS, A. T. (1957) *N.Z. J. Sci. Tech.*, **38A**, 908.

Acute Gastric Distension in Man and Animals

By NORMAN C. TANNER, F.R.C.S.
London

ACUTE gastric distension is nowadays rare in man, because of the ease with which excessive collections in the stomach may be vomited, passed into the duodenum, or aspirated by stomach tube. In gastroscopic examinations, we may spend the best part of ten minutes continuously introducing air into the stomach and, although the stomach may become very distended, no damage is done, for air escapes both into the duodenum and back along the side of the gastroscope.

Acute dilatation of the stomach used to be a greater problem than it is to-day. Moynihan (1914) devotes seven pages to the subject as a post-operative complication. He describes it as being of insidious onset a few days after operation. The outline of the distended stomach may be seen and he noted that on passing a stomach tube much gas and some thin grey fluid escape, but recollect on removing the tube. He remarked on the fluid loss which is associated with the condition.

Many possible causes were discussed, but in the main, paralysis from over-distension and other possible mechanical causes were suggested. Conner (1907) analysed 102 cases of this complication and found a mortality of 72%.

In treatment, Moynihan recommended intermittent use of the stomach tube (continuous gastric suction not being then in use) adoption of the prone position and, if that failed, gastrostomy or gastro-enterostomy.

Just after the Second World War, there were several records of acute dilatation of the stomach in starved prisoners who were suddenly given large meals of soup, potatoes, carrots, &c. (Markowski, 1947). These were followed by collapse and obvious gastric distension, usually with some vomiting. Stomach tube drainage with the patient in the left lateral position gave relief in most cases, after up to 8 l. (2 gallons) of food and juice was aspirated. Not much was air. Some required laparotomy when, as with Moynihan's series, it was seen that the dilatation involved the duodenum and often the upper jejunum. Gastric atony is said to be common in starved people and it is possible that malnutrition may play a part in predisposing the patient to it.

We do not see this condition very often nowadays. It is probable that as a post-operative complication it is due to overdistension, either by air-swallowing or drinking in the operative and post-operative periods when the stomach is paretic. At the period when gastric peristalsis normally returns after an operation, the overstretched muscle fibres fail to respond. Nowadays, a stomach tube is used prophylactically or very early when the condition is suspected, and so overstretching of the muscle fibres never occurs or is soon remedied.

During the last three years at St. James's Hospital, Balham, in a series of 3,000 autopsies, there were 2 cases in which acute dilatation of the stomach played some part in their deaths (Table I):

TABLE I

	Age	Sex	Pre-disposing	Time after injury or operation	Result
J. S.	40	M.	Fractured spine. Ruptured urethra	5 days	Died (inhaled vomit, acute gastric ulcer)
A. F. H.	57	M.	Operation for hiatus hernia	4 days	Died

Other cases have occurred post-operatively but have responded to aspiration treatment.

The only case of spontaneous acute dilatation of the stomach of which I have heard recently was one described to me by Wing Commander F. H. D. Hutter. He treated a case in an Air Cadet, aged 15 years, who collapsed with abdominal pain and at laparotomy was found to have acute gastric dilatation extending into the upper jejunum. He was treated by gastrostomy. The condition had caused very severe collapse post-operatively and he developed anuria. After an extremely difficult period urinary secretion was re-established and he finally recovered.

In intestinal obstruction, the stomach may become very distended with fluid and gas and swallowed air. This only becomes very troublesome if there is a paretic condition of the stomach preventing vomiting. Such a paresis may occur if there has been much previous fluid loss and potassium deficiency has resulted, or if the condition is a peritonitic or paralytic ileus.

Severe distension may arise if the patient is able to swallow air, but unable to eructate in the post-operative period.

A young man came under my care with a history of several years of epigastric discomfort immediately after swallowing. A radiograph showed a large diverticulum just below the cardia, the distension of which appeared to account for the symptoms. An operation was carried out to invaginate the diverticulum and repair the muscular defect. A curious effect followed. Within two or three days the abdomen was tensely distended with gas. On passing a large stomach tube, the gas escaped, with an audible hiss and relief to the patient. Unfortunately, he would not tolerate the tube and each time the tube was removed his stomach refilled with gas within a few hours. What had happened was that the invaginated diverticulum had become swollen and blocked the cardia like a ball valve, allowing swallowing but not the eructation of air.

This case demonstrated the large amount of atmospheric air which is normally swallowed and, presumably, normally eructated quietly. With the removal of the mechanism for expulsion, there was abdominal distension within a matter of hours. At a second operation, the stomach was seen to be greatly dilated, mainly with gas, much of which had entered the small bowel, and the congested, bruised, invaginated diverticulum was found obstructing the cardia, and so the diverticulum was removed.

In a second case, a patient had a gastric ulcer removed from the region of the cardia by gastrectomy by one of my registrars. After this, he suffered gaseous distension until he was relieved by passage of a stomach tube. An X-ray showed deformation of the lower œsophagus which produced an "S" bend similar to the "S" trap used by plumbers to prevent gases coming up from the drains. Fortunately, this condition righted itself spontaneously.

Gases other than atmospheric air may arise in the stomach, but rarely give rise to acute distension unless there is some obstruction. This may occur in cycles rarely after vagotomy or in patients with duodenal stenosis, in whom large quantities of food, juice, saliva and swallowed and chemically produced gas eventually lead to gastric distension and vomiting. That the gas is not entirely swallowed air is shown by the fact that two of my vagotomy and one of my stenosed duodenal ulcer cases have had mild explosions through the nares due to lighting a cigarette while eructating.

Acute distension may follow the swallowing of chemicals. I saw an interesting case of this nature on a visit to Johannesburg in 1950.

A young man desired an aperient and so took a Seidlitz powder. This powder consists of a blue packet containing sodium potassium tartrate with sodium bicarbonate, and a white packet containing tartaric acid. The two are put into a half pint of cold water, when much gas is given off and the fluid should be drunk while effervescing. This young man unwisely swallowed the acid first and then swallowed the bicarbonate, so that all the carbon dioxide was liberated in his stomach. He afterwards declared that his stomach exploded and that he was thrown against a wall. This was followed by severe abdominal pain and my ex-registrar, Mr. Leo Gottlieb, operated on him a few hours later and found a long tear in the stomach, unassociated with any ulcer. Fortunately, he made a good recovery after Mr. Gottlieb's repair of the tear.

Finally I would record that the stomach may also become acutely distended with blood in cases of hæmatemesis. While operating on such cases, I have noted the large amounts of blood and clot which may be present in the stomach, but again, a good vomiting reflex prevents overdistension. In one of my patients with a carcinoma near the cardia, which prevented efficient vomiting, the stomach ruptured during a hæmorrhage; a tear some 5 in. (13 cm.) long spreading from the edge of the carcinoma was found at subsequent laparotomy.

REFERENCES

CONNER, L. A. (1907) *Amer. J. med. Sci.*, **133**, 345.
MARKOWSKI, B. (1947) *Brit. med. J.*, ii, 128.
MOYNIHAN, B. G. A. (1914) Abdominal Operations. 3rd ed. London; **1**, 90.

Infections become

just a storm in a teacup

with ACHROMYCIN* V

BUFFERED TETRACYCLINE

*REGD. TRADEMARK

CAPSULES: 50 mg. Bottles of 25 and 100
250 mg. Bottles of 16, 100 and 1,000

SYRUP: Each teaspoonful (5 cc.) contains 125 mg. tetracycline HCl. Bottles of 2 fl. oz. and 16 fl. oz.

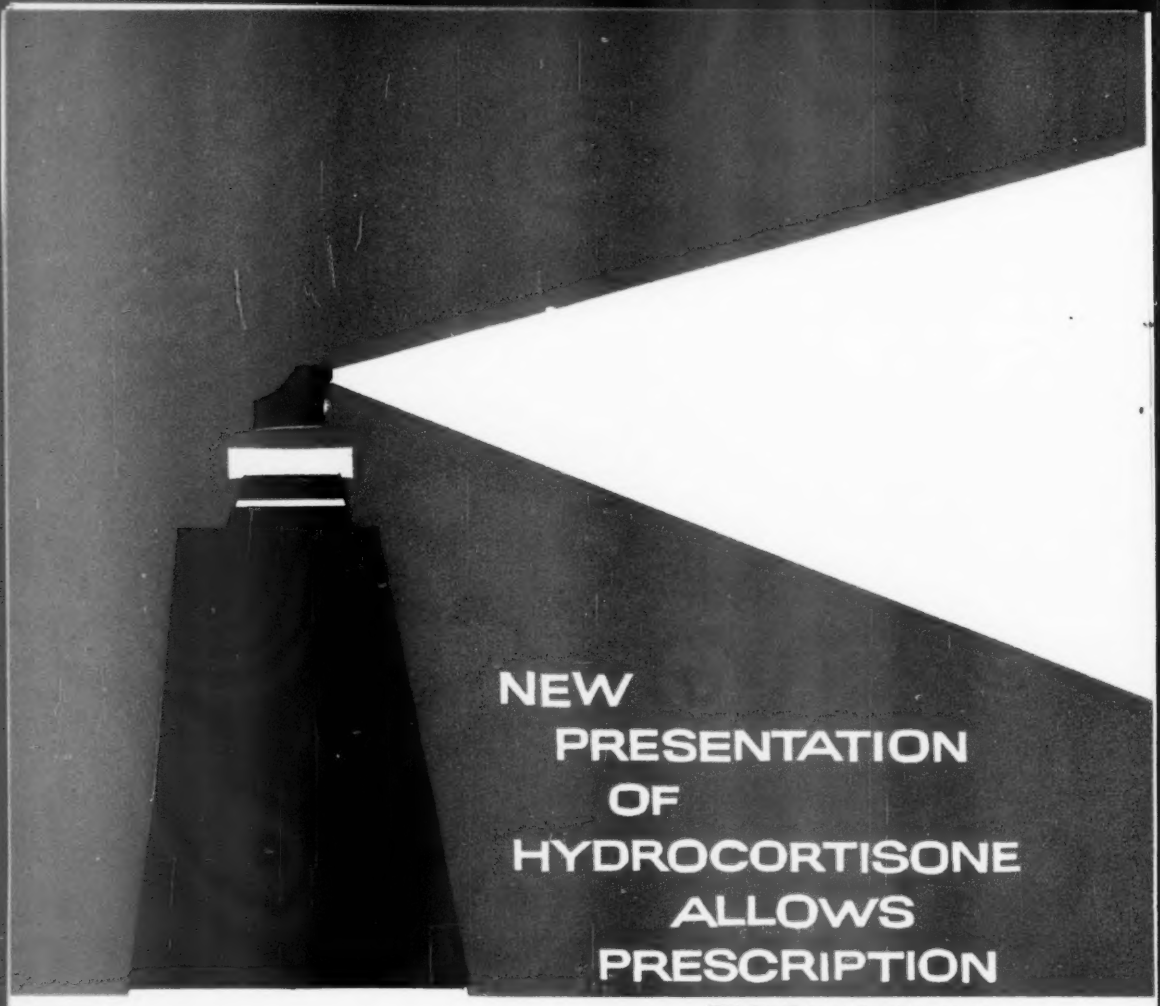
PEDIATRIC DROPS AQUEOUS: Each cc. contains 100 mg. tetracycline—approximately 5 mg. per drop. Plastic dropper-type bottle of 10 cc.

Within minutes... High blood levels for hours

Lederle

LEDERLE LABORATORIES
a division of
CYANAMID OF GREAT BRITAIN LTD. London W.C.2

CYANAMID



NEW PRESENTATION OF HYDROCORTISONE ALLOWS PRESCRIPTION ECONOMY

Cortril Spray adds economy to the proved effectiveness of topically applied hydrocortisone. It obviates experiments to find the correct presentation of hydrocortisone for a particular case. It saves the wastage of prescriptions part-used because of unsuitable strength or base. Cortril Spray is the only single preparation suitable for all non-infected dermatoses: moist and weeping or dry and scaling.

Cortril* spray

brand of hydrocortisone

PRESENTATION Plastic coated glass bottles containing 100mg. hydrocortisone free alcohol for spray application.

ADMINISTRATION Cortril Spray may be used four or five times a day until the inflammation subsides. For maintenance Cortril Spray should be used once or twice a day. The instructions on the pack should be noted by the patient: shake before use, keep away from direct heat, for external use only, do not spray near the eyes.

SCIENCE FOR THE WORLD'S WELL-BEING

Pfizer

Pfizer Limited, Folkestone, Kent

* Trade Mark

3185

Section of Pædiatrics

President—CHARLES PINCKNEY, F.R.C.P.

Meeting
December 10, 1958

Going to Hospital with Mother

A Documentary Film

By JAMES ROBERTSON
London

(In co-operation with staff, patients and parents at Amersham General Hospital, Bucks.)

MY first film "A Two-Year-Old Goes to Hospital," which was presented to the Section of Pædiatrics in November 1952 (Robertson, 1952; Bowlby and Robertson, 1953), has become a standard "text" in teaching units in many parts of the world. I welcome the opportunity to introduce its successor "Going to Hospital with Mother" (Robertson, 1958*a*).

It is now generally recognized that there is a special problem in the care of young children in hospital. The child of under 3 or 4 years is too young to be effectively prepared for going to hospital, a fact that is sometimes overlooked in leaflets issued by hospitals for the guidance of parents. He is intensely attached to his parents—particularly to his mother—and if going to hospital means leaving her care (which it usually does) he reacts with acute distress no matter how kindly he is cared for by doctors and nurses. The process of "settling down" is not to be taken at its face value. It is now common knowledge that even "settled" young children are on return home often anxious, insecure and difficult to manage; and that features of this disturbed behaviour quite commonly persist for weeks or months, and sometimes for much longer.

During recent years there have been many changes in the management of children's wards, intended to make a stay in hospital as happy as possible. There are more toys and playrooms, more freedom of movement and less concern about tidiness. There are also many hospitals which now allow parents to visit daily. But studies show that although these innovations are of considerable benefit to older children, greatly reducing the incidence of distress and disturbance, they are much less helpful to the younger ones (Robertson, 1958*c*). Despite daily visiting and associated amenities, children of under 3 or 4 years continue to react to hospitalization with distress, particularly to the separation from the mother that is involved, and with clinging and other signs of insecurity on return home.

It has been said that the greatest single cause of distress in young patients is not illness or pain but separation from the mother, and a growing number of children's wards are trying to meet the situation by allowing more or less unrestricted visiting. This is a great advance, but there is no doubt that from the child's point of view the optimum solution is that separation should be avoided by admitting child and mother to hospital together.

This is not a new idea. It is common practice in less developed societies and in those sections of civilized societies that can make private arrangements. But although Sir James Spence demonstrated its benefits at the Babies' Hospital, Newcastle upon Tyne, more than thirty years ago, there are to-day only a few wards within the National Health Service where some provision is made for admission of the mother. The method is slow to spread. There is a widespread disbelief in its practicability. Two main objections raised are that if mothers were admitted they would obstruct the efficient working of the ward by being anxious and interfering; and that it is not possible to accommodate mothers until special wards are built for the purpose.

In my new film it is seen:

(*a*) That if ordinary mothers are welcomed into hospital and given a positive role in the care of their sick children they generally respond by being as reasonable and adequate as they are in their own homes; that they are assets to the working of the ward and not nuisances; that there is a tremendous gain to the young child in having the mother with him while going through an experience of illness; and that the benefits of the method extend to mothers and staff.

(*b*) How the staff of one hospital have improvised a way of routinely admitting mothers with children under 5 years of age to a ward of

traditional design without making structural alterations.

The film is therefore not primarily about the mechanics of admitting mother and child though these are indicated. It is a study of human relationships—the relationship between a mother and child at home and in hospital; the relationship between the hospital staff and mothers who are admitted to help in the care of their children. It shows the serenity of the situation that is created, even when children are very ill.

I had waited a long time for the opportunity to make a film of this kind, and my main reason for deciding that Amersham General Hospital provided the setting I wanted was the fact that there *every* mother of a child under 5 years is invited to come into residence, with no attempt to discriminate between the "good" and the so-called "over-anxious" mother. This readiness to deal with a wide range of types and temperaments appealed to both my humane and scientific interest in the subject (MacCarthy, 1957; Robertson, 1958*b*, *c*).

In the Tavistock Child Development Research Unit we appreciate that admitting the mother to help in his care makes hospital a happier place for the young child and is fully justified on this score alone. But our chief reason for advocating this method of care—and my main reason for making this new film—is that the admission of child and mother together is a positive measure of preventive mental health. Separation from the mother can be traumatic and may leave long-lasting and possibly permanent emotional disturbances. The presence of the mother disposes of the dangers associated with separation, and helps to prevent anxieties arising from illness, pain, investigation, and operation from becoming cumulatively overwhelming.

At Amersham General Hospital the primary concern in admitting mothers was to prevent the unhappiness that is caused to young patients by separation from the mother. The possibility of after-effects or lasting harm from separation was a secondary consideration, though Dr. MacCarthy and his associates recognise how important these effects can be. Their case for having mothers to live in the ward with their children is mainly based on its obvious practical benefits and its humanity.

But although the emphases are different there is obviously much common ground in our mutual concern to find the best ways of dealing with young children in hospital. We hope that the making of this film as an example of profitable co-operation between the pædiatric department at a General Hospital and the psychiatric research unit at the Tavistock Institute of Human Relations will commend itself to pædiatricians and psychiatrists elsewhere.

The film is, of course, unrehearsed and unenacted. The principal child and her mother were next on the list for admission; the other children and mothers who are seen are those who happened to be there; and the staff are going about their ordinary duties.

Synopsis of the Film

The opening scene is the children's department of the hospital. In the open ward there are children over 5 years of age whose parents do not stay, but who may visit at any time and stay as long as they wish. The parents of these older children can give them personal attention—feeding, washing, haircombing, and so on.

Approaching the open ward is a corridor with the usual offices and duty rooms along one side and on the other a series of eight cubicles originally intended for the protection of small babies against cross-infection. To the cot and locker which are the usual furnishing of such cubicles have been added a bed for mother and an easy chair. The cubicles are glass-walled, and curtains can be drawn between them when privacy is wanted.

The film tells the story of one little girl and her mother, against a background of other resident mothers and their children. Sally is 20 months old, the second child in a working-class family. She is seen first in her home, a lively, mischievous little girl—full of activity, never far from her mother's skirts, impatient of interference. When her face is washed she resists and cries loudly, but the tears are dry in a moment. Her mother, busy about her domestic jobs, has the ordinary mother's competence in doing many things at the same time—including cooking the lunch and meeting her children's needs.

When Sally goes to hospital for a minor operation mother goes too. Sally's 4-year-old sister Angela is left at grandmother's house where she will stay in the daytime, going home each evening with father on his return from work.

At the hospital they are met by the Ward Sister who shows mother the amenities, including the kitchen. "There is the teapot, Mother, here is where the tea is kept—so have a cup of tea when you feel like it." Then she leaves them in their cubicle—10 × 9 ft.—containing a locker, a cot for Sally, a bed for mother, and a washbasin. As she hangs up her coat and settles in she can see through the glass walls the neighbouring mothers and their children.

When the surgeon calls to make a preliminary examination, Sally characteristically protests loudly at the interference; but with mother there

to hold her the protest is brief. Later, as she is tucked down for the night, talking up to her mother and full of fun, it is clear that it is the presence or absence of mother that matters to a child of this age and not whether her cot is at home or in hospital. That, of course, is the theme of the film.

Next morning Sally is prepared by Sister for the operation—skin cleansed and premedication given by mouth and injection. She is held throughout by her mother, whose lips press tightly together as she empathizes the reaction of Sally to the needle. Sally resists and cries, then cuddles down in her mother's arms. As the trolley wheels her away she stirs and comes to her knees, but mother is there with a gentle hand and a quiet word to soothe her. In a moment she is tucked down again and on her way to the theatre.

While the operation proceeds it is good for mother's morale that she can sit chatting to another mother in one of the cubicles.

Within a few minutes of Sally's return to the cubicle she has an injection to put her to sleep. Mother is reassured by Sister that all is well, and sits quietly beside her sleeping child.

As the film goes on, Sally is awake but not very well following the operation, and mother intuitively meets her needs for comfort—wiping her brow, smoothing back her hair, sitting quietly by. And at times when Sally is content to lie quietly mother is with her neighbour in the next cubicle—sharing a small job of making swabs for the hospital, enjoying a chat, and at the same time able to keep an eye on Sally through the glass wall and to go to her when she stirs.

Being unaccustomed to the aftermath of an operation, mother has moments of anxiety. The Sister and Registrar quietly reassure her. The atmosphere is permissive and supportive so that when the Consultant Surgeon visits on the third day to check up on his case mother feels she can talk to him freely about her anxieties; he too plays his part in reassuring and encouraging her.

So the days go quietly by, with mother initially under some strain but able to play her part with the unobtrusive support of staff who appreciate the value of her presence.

There are six other mothers in residence, and although the children of all of them are ill—some seriously—the morale of the mothers is high. It is high because they are able to help in the care of their children, to give each other friendly support and to work together doing odd jobs for the ward. And, equally important, because they are made to feel that the staff regard their presence as of great value to their children.

On the day following the operation, Sally is unwell and quiet; but as her physical condition improves so do her spirits. At no time does she show any of the fretfulness or withdrawal so commonly seen in unaccompanied young children. And on the fifth day, when she is fully recovered from the operation, she is as bright and mischievous as at home—and in a general state of good-humoured well-being which is *never* seen in unaccompanied children of this age on the fifth day in hospital. Lying on her mother's knee for a final napkin changing she is as secure and cheerful as when seen in the same situation at home at the beginning of the film.

On return home Sally showed none of the disturbed behaviour typical of young children who have been in hospital without their mothers. She took up immediately with her playmates, ate and slept well and had no temper tantrums. She acted as if she had never been away, as in a sense she had not since that part of her environment which mattered most had remained constant. The presence of her mother had converted going to hospital from a major event into a lesser experience of the kind that occurs within the security of the family and which young children take in their stride.

REFERENCES

BOWLBY, J., and ROBERTSON, J. (1953) *Proc. R. Soc. Med.*, **46**, 425.

MACCARTHY, D. (1957) *Publ. Hlth., Lond.*, **71**, 264.

ROBERTSON, J. (1952) Film: A Two-Year-Old Goes to Hospital. Tavistock Child Development Research Unit, London.

—— (1958*a*) Film: Going to Hospital With Mother. Tavistock Child Development Research Unit, London.

—— (1958*b*) Guide to the Film "Going to Hospital With Mother". London.

—— (1958*c*) Young Children in Hospital. London and New York.

DISCUSSION

Dr. Dermod MacCarthy:

The approach to the care of small children in hospital which is portrayed in the film began as an experiment. The experiment was to see whether the idea of keeping mother and young child together could be put into practice in an ordinary children's ward without special accommodation for mothers.

I would like to mention the things which influenced us towards making this experiment. I think I must put first the influence of the Newcastle School of Pædiatrics which I encountered in 1946. The Babies' Hospital was not actually functioning at that time, but I saw it later. Second I would put the more uncomfort-

able awareness of the distress of small children in hospital which comes with the spread of knowledge of child psychology generally, perhaps enhanced by having children of one's own. Mr. Robertson's first film "A Two-Year-Old Goes to Hospital" was a final and important influence prompting us to take some practical steps about the problem, though personally I went through an initial stage of antagonism to the concepts with which that film confronted us. We have since found ourselves better students and better observers of what is going on in the mind of a small child under conditions of maternal separation. Lastly, although our method was evolved primarily to remedy the immediate situation of the sick child, our frequent finding, in case histories, of disturbing hospital experiences strengthened our conviction that the aim was worth pursuing in spite of some difficulties.

Our early admission of mothers was tentative but the benefits were quickly apparent and before long we had learned the main lessons from it and it became an established practice.

When in 1956 Mr. Robertson suggested making a documentary film of this unit, which seemed to him to be successfully demonstrating the truth of views long held by the Tavistock Institute, we had been admitting mothers for three years. I felt we were ready, but only just. There was still a lot more to learn, as we have found since the film was made. I was very grateful to have the opportunity of getting this experiment illustrated through his special skill and experience. We have subsequently collaborated closely in shaping this film to convey the main theme—which is the complete acceptance of mothers as necessary for the small child's welfare in hospital (this includes physical as well as mental welfare) and the integration of the role of the mother with the nursing care of the child and the work of the ward.

It is a very big subject. The practical difficulties all in all may be held by some to outweigh the benefits claimed by those who have put these ideas into practice, but we have found none of these difficulties insoluble.

I would like to emphasize that the mothers who are admitted to the Amersham Unit (there have been over 500 of them now) are there because the opportunity is offered them and they feel it necessary to be there and worth while to make special arrangements for temporarily leaving their home. There is no coercion, they are a group self-selected by their sense of the importance of staying with their child. They number about half of the total of children admitted under the age of 5 years.

Reluctance to make provision in a children's ward for the presence of mothers day and night is still widespread, though showing signs of yielding. It is partly due to prejudices of the medical and nursing professions, but these I now believe go far less deep than has been supposed. It also derives from lack of correct observation and interpretation of the signs and symptoms of separation anxiety in children. One of the benefits of getting mothers into a general pædiatric ward is to improve people's observation by throwing into sharp contrast the state of the child who is alone and anxious, and the security of the one who has his mother.

Argument for and against the theme of this film ought to be based on a definition of the needs of a typical child and a typical mother. But one of the things that films bring home is that there is no such case. We are always dealing with individuals; and one who would appear not to fit into the scheme can always be found.

Meanwhile the benefits which result all round from avoiding "separations" can be achieved to a great extent, we feel, in any children's ward where the staff are ready to make a new acceptance of the importance of the mother to the small child, in illness as well as in health.

I wish to thank Dr. Mary Lindsay for all her help in the first three years of this plan, and Sister I. Morris, who, as the film shows, is the person on whom the whole scheme hinges.

Meeting
February 27, 1959

A DISCUSSION was held on **The Child Who Could Do Better at School.**

The opening speakers were Dr. A. DOYNE BELL, Mr. E. BLISHEN, Mr. H. A. T. CHILD and Dr. R. F. BARBOUR.

A PRODUCT OF RESEARCH

AVAILABLE FOR PRESCRIPTION NOW

ORAL IRON—A NEW PRESENTATION

FERROMYN
Capsules

Many constructive reports originating from doctors who are prescribing ***FERROMYN*** in many countries throughout the world sponsored the developments to improve its effectiveness still further. It became evident that it was necessary to present ***FERROMYN*** in a new form to achieve an even more rapid disintegration, coupled with increased stability.
During the past two years, tests have been carried out presenting Ferrous Succinate in many forms—***THE MOST SATISFACTORY OF WHICH HAS PROVED TO BE A CAPSULE.***

Providing these outstanding advantages:

(i) *ferric iron content is not more than 0.5 mg. and does not increase on prolonged storage.*
(ii) *disintegration is rapid (5 minutes).*
(iii) *intolerance is less than 1%.*
(iv) *haemoglobin response is 1%–2% per day*

FERROMYN (Ferrous Succinate), originated and developed in our own laboratories, is prepared from the mild, atoxic ferrous salt of succinic acid and is one of the most effective organic iron salts, requiring no other additives to produce a rapid haemoglobin response or to reduce the intolerance and side effects usually associated with oral ferro-therapy.

FERROMYN IN 3 FORMS: CAPSULES, TABLETS, ELIXIR

FORMULAE

FERROMYN
Each capsule/tablet/teaspoonful contains:
Ferrous Succinate . . . . . 150 mg

FERROMYN 'B'
Each capsule/tablet/teaspoonful contains:
Ferrous Succinate . . . . . 150 mg.
Aneurine Hydrochloride . . . . . 1 mg.
Riboflavin . . . . . 1 mg.
Nicotinamide . . . . . 10 mg.

DOSAGE
one capsule, tablet or teaspoonful between meals or as prescribed.

PRESENTATION

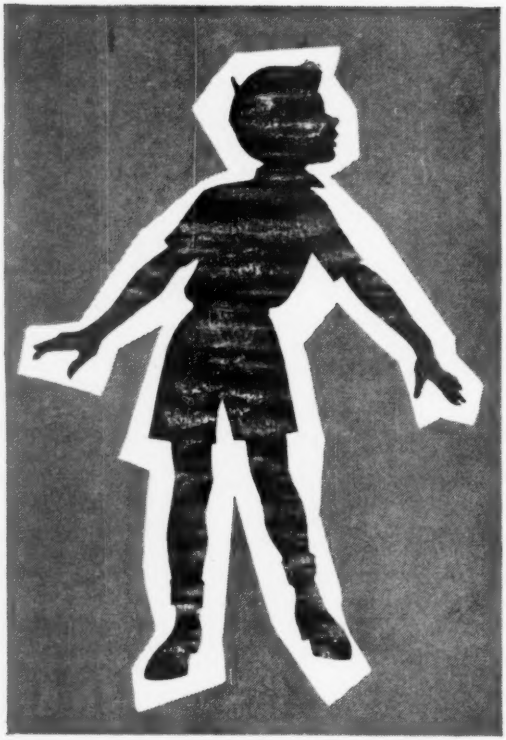
FERROMYN Capsules / Tablets — Packs of 100 and 1,000
Trade Price
100 capsules/tablets 3/- + p.t.

FERROMYN Elixir
Bottles of 4 ozs. and 20 ozs.
Trade Price
4 oz. elixir 4/3d. + p.t.

FERROMYN 'B' Capsules / Tablets — Packs of 100 and 1,000
Trade Price
100 capsules/tablets 3/9d. exempt p.t.

FERROMYN 'B' Elixir
Bottles of 4 ozs. and 20 ozs.
Trade Price
4 oz. elixir 4/6d. exempt p.t.

CALMIC purely British Pharmaceuticals
CALMIC LIMITED · CREWE HALL · CREWE · CHESHIRE · Crewe 3251/7



resistant
EPILEPSY
responds
well to-

DIAMOX*

ACETAZOLAMIDE

Of all the applications of DIAMOX acetazolamide, few are more welcomed in clinical practice than is its value in epilepsy. Freedom from epileptic seizures has been observed in numerous cases of grand and petit mal following treatment with DIAMOX. The drug has shown an unusually beneficial effect on resistant cases of petit mal. It is effective when used alone and of particular value when used in combination with the usual anticonvulsants. Highly versatile, DIAMOX has long been recognised for its value in other conditions including cardiac oedema, glaucoma, premenstrual tension, toxaemias and oedema of pregnancy, drug-induced oedema, etc.

TABLETS: *Diamox Acetazolamide Tablets of 250 mg. (engraved). Packing and basic N.H.S. cost: Bottles of 25, 13/10. 100, £2.6.6. 1,000, £21.9.10.*

PARENTERAL: *Diamox Acetazolamide Sodium Parenteral 500 mg. Packing and basic N.H.S. cost: Vials of 500 mg. 18/-.*

*REGD. TRADE MARK

Lederle

LEDERLE LABORATORIES
a division of
CYANAMID OF GREAT BRITAIN LTD. London W.C.2

CYANAMID

Section of Proctology

President—HENRY R. THOMPSON, M.A., M.B., F.R.C.S.

Meeting
January 14, 1959

Intra-abdominal Repair of Rectal Prolapse in Women

By E. C. B. BUTLER, F.R.C.S.

London

Definition.—Complete rectal prolapse in women may be defined as a sliding hernia through the pelvic floor, the sac being situated between the rectum and vagina.

Ætiology.—In many cases the ætiology is obscure. In this series a definite cause was only found in 4 patients: 1 had a spina bifida occulta; 2 had been operated on for tumours of the cauda equina; and 1, a girl of 17, was said to have had meningitis as a child. In the remainder, one could only postulate an abnormally deep recto-uterine pouch. If the intra-abdominal pressure rises or the pelvic floor weakens in such patients, it can be seen how this deep pouch can become a hernia and eventually present at the anus as a typical rectal prolapse.

Age.—This condition may occur at any age; the youngest here was 17, the oldest 76.

Some of these patients may become mentally deranged, and one in this series was operated on in a mental hospital; the functional result was good, but the mental state was not improved.

Diagnosis.—This is usually obvious and it should always be possible to control the prolapse by supporting the anterior rectal wall with two fingers in the rectum.

Investigations.—The lumbar spine should be X-rayed, in order to exclude an unsuspected spina bifida; this is particularly important in young patients. The perineum must be carefully examined, as an old laceration of the sphincters or perineum may need repair after the prolapse has been controlled. Uterine or vaginal prolapse should be looked for, and the help of a gynæcologist enlisted if thought expedient.

Treatment.—The only satisfactory treatment is surgery; but minor degrees of prolapse in elderly women may be partly controlled by a Thiersch operation.

Operative procedures.—When it was recognized, first by Moschowitz (1912) and later by Roscoe Graham (1942), that rectal prolapse was really a form of hernia, the abdominal route became increasingly popular, as it is impossible to remove completely the hernial sac from below, which doubtless accounts for the high recurrence rate following the operation of perineal recto-sigmoidectomy.

I now carry out two operations for prolapse:

(1) Intra-abdominal repair without excision of the excess bowel.

(2) Intra-abdominal repair combined with rectosigmoidectomy from below.

Either procedure may be accompanied by some form of perineorrhaphy either at the same time or at a later date, should the sphincters be torn or injured.

I have had no experience of abdominal repair combined with restorative resection, but the results as reported by Muir (1955) are good.

STEPS OF THE OPERATION (ABDOMINAL REPAIR)

(1) The patient is placed in the lithotomy Trendelenburg position and, after laparotomy, the intestines are packed out of the pelvis and the extent of the hernial pouch demonstrated by a hand in the hernial sac, which extends well into the prolapsed bowel.

(2) Two sutures are placed in the uterus, if present, and it is drawn aside by an assistant, who stands between the legs.

(3) The whole of the hernial sac is excised: in these patients the peritoneum is usually thin and the course of both ureters can clearly be seen before the peritoneum is incised.

The sac is removed in two sections on either side of the rectum, care being taken not to injure the anterior rectal wall. The posterior wall of the vagina is thus completely denuded of peritoneum, but the bowel still has its covering anteriorly. When this has been accomplished the true pelvis should be denuded of peritoneum.

(4) The rectum is then mobilized posteriorly and laterally down to the pelvic floor, but no attempt is made to approximate the atrophic levator muscle, as practised by Goligher (1958).

(5) The rectum is next pulled up and sutured to the posterior wall of the vagina by interrupted thread or silk sutures, so that the rectovaginal septum is reconstituted.

(6) The peritoneal floor is then reformed at the pelvic brim.

(7) The abdomen is closed and a ventrofixation of the uterus is performed. If the patient has previously had a hysterectomy the vaginal vault is tethered to the anterior abdominal wall by stout silk sutures. The object of these steps is to fix the vagina until such time as the rectum and vagina have become adherent. Similarly, it is hoped that the back of the mobilized rectum will become adherent to the anterior surface of the sacrum.

After the operation, the foot of the bed is kept raised for two weeks, and the patient not allowed out of bed until the third week.

Results

19 patients have been treated by this operation since 1947; 6 of these also had a perineorrhaphy at the same time or later, which was carried out by Mr. R. A. Brews, and one patient is being treated by Mr. Charles Heanley for a complete tear of the sphincters.

3 cases have relapsed; 2 were treated by a combined abdominoperineal rectosigmoidectomy in 1952 and 1953 and remain well. The other patient, a girl aged 18, had a recurrence after nine years and will shortly be readmitted for further surgery.

8 patients had their operations over five years ago and only one of them has a recurrence. One patient has died of cancer.

One women, aged 53, had a bilateral ureterocolic anastomosis in 1955 by Professor V. W. Dix for chronic interstitial cystitis. For three months she had an increasing prolapse. 12.8.58: Laparotomy showed that the site of the bilateral ureterocolic anastomosis was normal; the usual operation was carried out with ventrofixation. Following operation the tone of her sphincters has very much improved and her control is adequate, although she has her bowels open once an hour.

Combined Abdominoperineal Repair with Rectosigmoidectomy

This operation is carried out in patients who are physically fit if the prolapse is very big, or if the prolapse has recurred after a previous operation.

Steps of the Operation

(1) Up to stage 4 of the previous operation the procedure is similar. If an excision is thought necessary, a second surgeon pulls out the excess bowel from below and performs rectosigmoidectomy, the anastomosis being carried out with two layers of sutures, the first, of interrupted thread, approximates the seromuscular coats, and the second, of interrupted catgut, unites all coats.

(2) It is important that at least 3 in. (7·5 cm.) of rectum be preserved, in order that the patient may keep her rectal sensation and preserve her continence.

(3) After the anastomosis, the suture line retreats inside the anus, the peritoneal floor is reformed, and finally a ventrofixation of the uterus is carried out.

Results

10 cases have been operated on since 1952, 5 of them over five years ago. So far, none has recurred, but one patient has died from cancer of the lung.

The functional results have been good. None proved fatal. One woman has had a baby by Cæsarean section and remains well.

There have been some serious complications:

(1) *Secondary hæmorrhage.*—2 patients had severe secondary hæmorrhage from the suture line, which required an emergency transverse colostomy with packing of the rectum. Both patients survived and their colostomies were later closed. It is interesting that secondary hæmorrhage is a recognized complication following rectosigmoidectomy but is almost unknown after restorative resection.

(2) *Rectovaginal fistula.*—One woman developed a rectal stricture at the site of the anastomosis following an abscess above the stricture, which burst into the vagina. A colostomy was carried out, then an internal proctotomy, and later closure of the colostomy. She is now well.

(3) *Pelvic abscess.*—In one patient a pelvic abscess formed which required a temporary colostomy for a few weeks.

Conclusions

(1) Rectal prolapse in women should be regarded as a sliding hernia, and its treatment should include excision of the sac.

(2) The operation of choice in this series was excision of the sac from above, reformation of the rectovaginal septum and ventrofixation of the uterus.

(3) In severe or recurrent cases, excision of the redundant bowel is indicated; this may be done from below (rectosigmoidectomy) or from above (restorative resection).

(4) The late results and complications of 29 cases operated on between the years 1947–58 have been described.

REFERENCES

Goligher, J. C. (1958) *Brit. J. Surg.*, **92**, 323.
Graham, R. R. (1942) *Ann. Surg.*, **115**, 1007.
Moschowitz, A. V. (1912) *Surg. Gynec. Obstet.*, **15**, 7.
Muir, E. G. (1955) *Proc. R. Soc. Med.*, **48**, 33.

New Operative Procedure for Complete Prolapse of the Rectum [*Summary*]

By D. W. Bracey, Ch.M.
Peterborough

Aim of operation.—After mobilizing the rectum and excising the peritoneal hernia, to draw the sagging and separated puborectalis muscles together and upwards by means of fascial strips.

Incision.—Transverse suprapubic.

Procedure.—(1) One 7 in. (17 cm.) strip from each external oblique aponeurosis tethered at the symphysis pubis is guided through the respective external abdominal ring and the immediate posterior wall of the inguinal canal on each side.

(2) After separating the rectus abdominis muscles in the mid-line and exposing the bladder retroperitoneally, the abdominal cavity is opened and the strips at each side guided down caudally and retroperitoneally along the lateral sides of the bladder to enter the pelvic cavity just above the ureters. From this point each strip crosses to the opposite side of the pelvic cavity and, after mobilization of the rectum and elimination of the peritoneal sac, the puborectalis muscles are defined on each side. Each strip is then threaded through the opposite puborectalis muscle just in front of the rectum at the level of the internal sphincter (Fig. 1). The strips are then pulled tight (Fig. 2), causing the two halves of the levator ani to come together, upwards and forwards. The ends of the strips are tied or sutured together, the peritoneal floor of the pelvic cavity reconstituted and the abdomen closed.

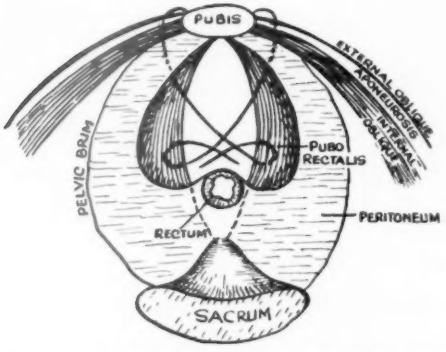


Fig. 1.—Showing the course of the strips before they are pulled tight.

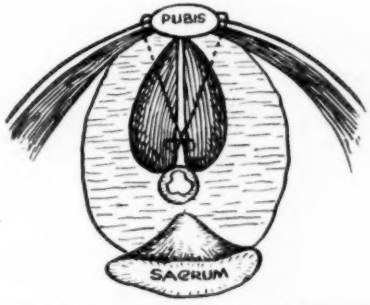


Fig. 2.—The strips pulled tight, tied or sutured and drawing the levator ani both together and upwards.

One case has been tried recently and so far the result is excellent, and it is hoped to render a follow up report of this case to the Section at a later date.

The Development of Carcinoma of the Large Intestine in Ulcerative Colitis [*Summary*]

By I. M. P. Dawson, M.D., M.R.C.P., and J. Pryse-Davies, M.D.
London

This brief report is part of a more detailed study (to be published later) of 663 patients with ulcerative colitis who have attended the Gordon Hospital between April 1947 and December 1958. During this period 15 patients with histologically proven ulcerative colitis developed confirmed carcinoma of large bowel; 2 further patients with proven ulcerative colitis were found to have metastatic carcinoma of probable large bowel origin. In view of the small number of cases with carcinoma and the short time available for follow-up, statistical conclusions are not yet

valid. We feel that certain features of these 17 cases (a crude incidence of 2·6% in this series) are worth reporting.

The average duration of ulcerative colitis before the discovery of carcinoma was 18·2 years, ranging from two to twenty years. Symptoms had commenced more than ten years previously in 13 patients. All the patients had histological evidence of ulcerative colitis with repair and fibrosis. Acute lesions were not a feature. The average age at the time of cancer diagnosis was 44·7 years with a range of 24 to 63 years; 5 patients were less than 35 years of age. In 9 patients carcinoma was confirmed in the rectum or rectosigmoid region, in 6 patients the growth was found elsewhere in the colon, while in 2 cases the site was uncertain. In only one instance were two separate carcinomas discovered, both occurring in the colon.

No diagnostic clinical picture was present at the time of cancer development. New symptoms such as abdominal pain and distension, altered bowel habits and rectal bleeding were described and some of the patients were found to be anæmic and to have lost weight. However, these features might have arisen in the natural course of their disease without the complication of cancer.

The prognosis in these patients was poor; 12 are dead and 1 patient is known to have secondary growth. 8 patients died within one year of the discovery of carcinoma.

12 patients underwent large bowel resection and 5 were deemed inoperable. Examination of the operation specimen showed that pre-existing fibrous stricture was present in 7 cases; in 3 cases it was difficult on examination of the surgically removed bowel to determine the site of the primary growth. Mucus secretion was a feature in 12 of the 17 cases and early spread in the serosa was common. Another feature was the tendency for individual islands of carcinoma in submucosa and muscle coats to become surrounded by fibrous tissue.

Polyps of various types were seen in 11 cases in the neighbourhood of the growth. It is normally easy to differentiate pseudopolyps, true adenomatous polyps and papillomas, but we found considerable difficulty in classifying some of the polyps examined. Appearances suggested that pseudopolyps could either directly undergo malignant change or develop into true adenomas which in turn might become malignant.

Congenital Rectal Prolapse

By Tom Rowntree, M.Chir., M.S., F.R.C.S.
Southampton

In the Maternity Department of the Southampton General Hospital in 1956 was born a 9 lb. girl, the second child of a 29-year-old mother. I was asked to see her because she was thought to have a polyp protruding from the anus. There was indeed a polypoid mass at the anus, but the orifice itself was contracted by a stricture that would not admit the tip of the little finger. The stricture was dilated quite easily after a few days and then the anus could be examined accurately. Fig. 1 shows the outer aspect of the mass; it occupied one-third of the circumference of the anus and its outer aspect was covered by the normal constituents of the anal canal, namely anal skin and mucosa of the correct colour, with columns of Morgagni and valves. The anal mucosa joined rectal mucosa in the normal manner, and the inner surface of the mass, seen in Fig. 2, was covered by normal-looking rectal mucosa. In Fig. 2 is seen a probe indicating the centre of the anal orifice. Fig. 3 illustrates part of the scar, on the stretch, which had formed the stricture. The scar extended throughout that part of the circumference of the anal orifice that was not occupied by the protrusion. The remarkable thing about the

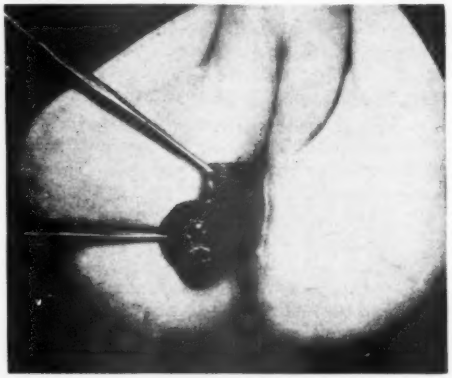


Fig. 1.—Outer aspect of the protrusion.

FIG. 2.—Inner aspect of the protrusion.

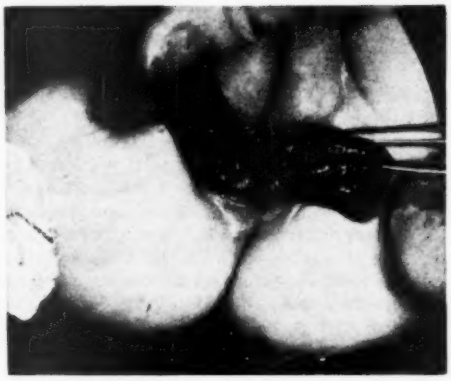


FIG. 3—The scar can be seen on the stretch as a white line.

circumferential scar was that it united perianal skin directly to rectal mucosa with no intervening anal epithelium whatever. It looked as if a Whitehead's operation had been performed. The underlying sphincter was normal according to digital palpation, and subsequent events have shown the girl to be continent.

The photographs were taken at the age of 6 months, just before operation, but there had been no change in the appearances in the interim save for dilatation of the stricture. Excision was necessary, for replacement of the protrusion was of course impossible. Fig. 4 shows the mass in transverse section. The epithelial elements can be recognized, with columnar epithelium on the inner side and specialized anal epithelium on the outer side, and even some anal glands. Between the two epithelial layers can be seen layers of muscle, indicating that the specimen consisted of a full thickness of bowel folded upon itself.

Considered alone, the specimen amounted only to prolapse of a portion of the rectum and anal canal. But how can the scar and the absence of the rest of the anal canal be accounted for? If there had been malformation there would be no scar, for a scar can only form when there has been solution in continuity in an epithelial surface. There must therefore have been some tissue formed which was subsequently lost. The explanation I put forward is that the entire rectum and anal canal were formed normally, but that there had been complete prolapse *in utero*, and the missing two-thirds of the circumference underwent aseptic necrosis (sloughing in a sterile medium). Repair quickly followed, all complete before birth, and soon enough for the scar to have contracted to form the stricture.

Tags of rectal mucosa are seen occasionally outside the anus at birth, but I have found no reference to a case which exactly tallies with this one. I have put the case forward as an example of complete rectal prolapse *in utero*, but I have no explanation to offer for the occurrence of the prolapse nor can I explain the hypothetical necrosis. I hope I will not be criticized for arriving at this conclusion on insufficient evidence of one case.

FIG. 4.—Arrow points to anal gland.

I thank Dr. R. A. Goodbody for the microphotograph.

Primary Pruritus Ani

By F. Austin Henley, F.R.C.S.
London

For the purposes of this communication secondary pruritus is excluded, for here the cause is apparent and when corrected the condition is eliminated.

In the investigation of more than 100 cases of primary pruritus ani, certain phenomena were recurrent in all cases. They were all fæcal retainers. By this term is meant that they all had loaded rectums and left colons, but the fæces were not necessarily hard. These patients had a bowel action once, twice or even three times a day. Each time the stool is normal and when questioned about the intake of aperients, they invariably reply: "I never need them as my bowels act every day and often more than once."

Now the reason that such patients have more than one daily bowel action is because they never adequately evacuate the rectum and sigmoid colon. If they retain 50% or 25% of the fæces in the left lower colon and rectum, it can readily be appreciated that without the use of aperients this residuum will build up daily so that there is ultimately a state of colonic retention.

Where colonic retention exists fæcal decomposition and gas formation become excessive, and it is this excessive passage of anal flatus which is the direct causative factor in primary pruritus ani. The flatus soils the underwear. The soiled underwear, with or without the sweat of the natal cleft, irritates the anal and peri-anal skin. Certain skins appear to be more sensitive than others, and particular types of materials used for underwear may be more prone to aggravate the irritation once it has begun. It is this combination of fæcal retention, anal flatulence, soiled underwear and lack of personal hygiene that is responsible for primary pruritus ani.

Treatment

Treatment is directed under three headings: (1) Dietetic; (2) Regimental; (3) Specific.

Dietetic.—These patients must avoid all flatus-forming foods. Onions, peas, beer in some patients, spirits in others, are the common examples.

Once the condition has been rectified they may resume the normal intake of these foodstuffs.

Regimental.—Personal hygiene is absolutely essential.

A daily morning action should be followed by bathing, and where this is not possible the anal area must be sponged with warm water and dried thoroughly. No dusting powder is necessary but can be added provided it assists the comfort and does not cause irritation.

Many patients with this complaint have their bowel action in the evening. These must alter their regimen to the morning, as the retention of fæces in the rectum all day leads to excessive flatus discharge, and no amount of local applications will eliminate the pruritic condition.

A fresh set of underwear daily is important.

Specific.—The first essential is to evacuate the bowel completely. Glauber salts or one of the other saline aperients is suggested, because in adequate dose it gives several actions, the last being a watery evacuation. It is then, and then only, that the colon is really clear.

Unguentum hydrocortisone 1% should be applied to the irritated area only for the first three nights after the commencement of treatment. This will break the scratching habit by relieving the irritation, and allow healing. It should not be necessary after this time.

At the time of the first consultation the pile-bearing area should be injected with 5% phenol in almond oil, as this relieves any excessive mucus discharge.

Provided that the patient adheres strictly to these instructions, the condition of primary pruritis ani will disappear. To prevent its recurrence an adequate dose of Glauber salts should be taken at least once a month to prevent colonic stagnation.

(*Meeting to be continued*)

BOOK REVIEWS

The Adoption of Inoculation for Smallpox in England and France. By Genevieve Miller. (Pp. 355; illustrated. 49s.) London: Oxford University Press. 1957.

Whatever shortcomings there may be in the author's style and manner of presentation, her subject is of the greatest interest and she has collected information on it with immense industry and care. The introduction into this country of inoculation against smallpox during the first half of the eighteenth century was an important step towards the scientific control of disease but probably few, even of those concerned with preventive medicine, will have more knowledge of the subject than perhaps some vague recollection of the name of Lady Mary Wortley Montagu. Even the part played by this lady was, we find, much less important than that of many others who have been forgotten.

In these days of controlled trials of vaccines with their ethical and other problems it is fascinating to read of the experiments on prisoners in Newgate Jail in 1721, and the attempts at statistical appraisal of the results of inoculation by the Royal Society in Newton's day. One may well ponder over the reasons why only one among so many intelligent men should have questioned the comparability of fatality rates from smallpox in the general population and those resulting from the inoculation of selected patients. The social and medical reasons why inoculation was accepted in England, but only much later in France, are analysed and there is an excellent account of the theories then held on the causation of smallpox.

Perhaps because inoculation has so often been dismissed briefly in the introductory sections of histories of vaccination, the author may have chosen to mention vaccination with equal brevity in this book. The relation of the one to the other could with advantage have been examined more fully.

The Organic Psychoses. A Guide to Diagnosis. By John G. Dewan, M.A., M.D., Ph.D. Cantab., D.P.M.Eng., F.R.C.P.(C.), F.A.C.P., F.A.P.A., and William B. Spaulding, M.D., F.R.C.P.(C.). (Pp. xiii + 170. 48s.) Toronto: University of Toronto Press. London: Oxford University Press. 1958.

This book is written primarily for hospital resident doctors but is addressed also to all doctors bewildered by the difficulties of this branch of medicine and to psychiatric nurses and social workers and psychologists.

It is a guide and is not intended to be an encyclopædic textbook, but aims to simplify the problems of diagnosis in patients having symptoms of "organic" type. A straightforward ætiological classification of organic psychoses is followed by a section in which the diseases are briefly described. The authors are aware that this section may be criticized as being too sketchy; taken by itself it certainly is but used in conjunction with larger texts and as a guide to the post-war literature in English, it will be of value to psychiatrists in training, quite apart from its obvious use, suggested by its synoptic form, in preparing for the D.P.M. examination. The second half of the book is largely devoted to the clinical description of 25 illustrative cases. The final chapter lists appropriate diagnostic investigations. There is a good index. The price seems exorbitant.

The Neurologic Examination. By Russell N. DeJong, M.D. 2nd ed. (Pp. xv + 1078; illustrated. £7 0s.) London: Pitman Medical Publishing Co. Ltd. 1958.

The title of this massive tome of over a thousand pages is not adequate to describe its contents, for it corresponds to such a work as Déjerine's "Sémiologie des Affections du Système Nerveux", which a generation ago was the standard work of its kind, and is still unsurpassed.

Professor DeJong's work is a compendium of the anatomy and physiology of the nervous system, together with an account of all the known physical signs and syndromes of nervous disease. In addition to this, it does contain detailed instructions upon clinical methods of examination as its title indicates, and includes such methods as perimetry and the examination of the cerebrospinal fluid. Finally, it contains accounts of named clinical entities or "diseases".

It is, therefore, in its way, a manual of nervous diseases, and thus far more than a guide to the examination of the nervous system. Its details are so numerous and comprehensive that it will prove a useful work of reference for the postgraduate student of neurology, and for the professed neurologist, but not for students and practitioners as the author suggests.

Its physiology is its weakest point. As far as the brain is concerned the author gives us something of everything that has been said—most as a result of animal experiment, which cannot be directly or without qualification applied to man—and reveals the fearful confusion into which the experimental physiology of the cerebral cortex fell during the years between the two wars.

In short, this work is the product of an inability to leave anything out, that is, to select. Its price will, of course, effectively inhibit its use by students in this country.

Thirst: Physiology of the Urge to Drink and Problems of Water Lack. By A. V. Wolf, Ph.D. (Pp. x + 536; illustrated. 95s.) Springfield, Ill.: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1958.

Although a sensation known to every man, thirst is a phenomenon which still defies exact analysis and explanation. In this monograph Dr. Wolf surveys all that is known about the subject. Beginning with a description of the fundamental aspects of body fluid metabolism, he passes on to consider the various theories of thirst, its place in the control of fluid balance, its effects, and its manifestations under conditions of extreme deprivation. There is a large section on the problem of the use of sea water to relieve thirst, and the book ends with several lengthy, verbatim accounts of men who have suffered severe water deprivation both at sea and in the desert.

Encyclopædic rather than critically selective, this monograph contains a vast amount of information on the subject, together with a very extensive bibliography. The ordinary medical reader will find this book indigestible fare, but to those interested in this particular subject or in the more general subject of body fluid balance it provides a comprehensive review and should prove a useful reference work.

Medulloblastoma. By Benjamin L. Crue, Jr., L.C.D.R., M.C., U.S.N. (Pp. x+206; illustrated. 43s.) Springfield, Ill.: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1958.

This monograph comprises an extensive review of the literature on medulloblastoma and, as the author states in his introduction, contains little that is new. The first half is devoted to a brief summary of present-day theories of the causation of malignant disease, followed by a description of the natural history of the tumour, and a discussion on its pathogenesis. Consideration is given to other brain tumours which may resemble it morphologically and which give rise to problems of histological diagnosis and of classification. The rest of the book deals with the clinical aspects of medulloblastoma. Considerable space is given to assembling the details of age and sex incidence from published series of cases. A graph based on 446 cases reveals a high incidence between the ages of 3 and 9. The chapter on symptoms and signs contains no particular noteworthy point, though enlargement of the head in a child should lead one to suspect a more benign cause for hydrocephalus than medulloblastoma. The occasional occurrence of this tumour in an adult is recognised, and that it then usually gives a rather different clinical picture. Treatment most favoured is a suboccipital decompression and biopsy, followed by radiotherapy. The results from various centres are quoted, the best being 7 survivors (for periods of from six to eleven years) of a series of 25. The illustrations comprise a considerable number of graphs and tabulated details; there is an extensive bibliography. It is an expensive little book.

Manual of Chest Clinic Practice in Tropical and Sub-tropical Countries. By A. J. Benatt, M.D. (Pp. vii+100; illustrated. 10s. 6d.) Edinburgh and London: E. & S. Livingstone Ltd. 1959.

In Britain there exists a wide network of chest clinics usually adequately staffed and equipped to make some impression on the dwindling tuberculosis problem. It is thus difficult for us to appreciate the difficulties still facing physicians struggling with tuberculosis in less fortunate countries. Alfred Benatt dedicated the latter part of his life to this struggle and his very practical conclusions based upon sound principles are behind this readable small volume.

The text is simple, short and always to the point; the author never loses sight of basic principles, yet gives the necessary practical details to enable instructions to be carried out sensibly. Sound advice is given on routine organization of clinic procedure, prevention of further infection, and treatment of the patient. The management of specific problems relating to diabetes and pregnancy in tuberculous patients is discussed. In the second part of the book reliable, simple techniques for collecting and investigating sputum and urine are well described; tuberculin testing and BCG vaccination are adequately dealt with and an appendix describes equipment and its care.

Apart from the usual small crop of printer's errors, criticisms can be few. For treating spontaneous pneumothorax polythene tubing would be simpler and cheaper than the Morland retention set; many physicians would object to the use of morphia, even in small doses, for hæmoptysis; there seems little point in delaying the BCG vaccination of newborn infants for six weeks; the keeping properties of liquid vaccine are exaggerated—it would be wise to use this only within a fortnight of manufacture. The discussion on the significance of the tuberculin test and the reaction to tuberculo-protein might be a little confusing to some readers.

But these are minor criticisms of an excellent practical, readable manual. As a guide for personnel of anti-tuberculosis departments in needy and perhaps less educated communities it should be invaluable and could be read with great benefit by nursing and health visitor staffs of chest clinics in this country.

Highlights of Ophthalmology. By Benjamin F. Boyd, M.D. 2nd ed. (Pp. xix+281; illustrated, with 36 plates. $9.) Panama, Box 1189. 1958.

This book represents a departure in medical publication. Professor Boyd, himself a leading ophthalmologist, attending the major ophthalmic congresses throughout the world, speaking several languages and personally known to most of the leaders of ophthalmology, seeks in this book to represent the trained ophthalmologist and his reaction to papers and discussions.

In Part I papers and discussions at the Pan-American Congress 1957 and at the Chicago Ophthalmological Society Meeting 1957 have been selected and their authors have contributed a new and somewhat condensed article to this book. This has been followed by a personal interview with the author wherever this has seemed necessary. The survey of current work is divided logically into symposia on surgery, therapeutics, vascular diseases, diseases of childhood and endocrine exophthalmos. This is followed by special reports upon technical procedures or points of particular interest.

In Part II a similar approach is applied to the surgery of detachment of the retina. Here Professor Boyd, with Dr. John McLean and Dr. A. E. Maumenee, examines in some 67 pp., lavishly illustrated with beautiful line drawings, the whole concept of the management and treatment of the retina. This is a most stimulating and authoritative contribution. It is followed by a limited but valuable examination of current problems in glaucoma.

Part III is a series of personal interviews: the particular problems of glaucoma in negroes are examined—subsequent sections deal with special problems of current importance.

It follows from its conception that this book contains no index apart from its Table of Contents, and no references in the course of the presentation of its material. None the less the contents are very clearly set out. It is easy to pick out material of particular interest and, notwithstanding the diversity of authorship, the editor has produced a book which is uniform in its writing, in its presentation and in the excellence of its contents. It is well printed and the illustrations are exceptionally clear. The text is notably free from defects of spelling or printing.

"Highlights of Ophthalmology" is throughout alive, unusually well informed, topical and stimulating. It is a book for the practising ophthalmologist rather than for the student, bringing to ophthalmic literature many of the qualities of a newspaper in that it is entirely current in its concerns and largely employs the technique of reporting. As evaluation proceeds the greater part of its contents will pass into the textbooks or will be discarded, but in a subject which is advancing on so many fronts so rapidly this up-to-date interpretation is invaluable. It represents a new approach which may well be applicable to other departments of medicine.

Recent Studies in Epidemiology. Edited by J. Pemberton, M.D., M.R.C.P., D.P.H., and H. Willard, M.D. (Pp. xiii+203; illustrated. 25s.) Oxford: Blackwell Scientific Publications. 1958.

The 18 papers in this book were presented at a meeting of an international Study Group on Preventive and Social Medicine held in Holland in September 1957. They deal with various aspects of recent epidemiological research, largely in the non-infective diseases. The papers fall into 6 groups dealing with: (1) use of existing records; (2) the *ad hoc* survey; (3) epidemiology in less developed areas; (4) mental illness; (5) evaluating health needs; and (6) general practice. The general conclusions from the papers and from the Group's discussions of them are very usefully summarized in a chapter of 12 pages. Among the problems that were the subject of the surveys are: the risk of cancer from work in nickel refining and following therapeutic or diagnostic radiology; bronchitis and other respiratory diseases; ulcerative colitis and infective hepatitis; heart disease, and mental disease.

The book is one that can be thoroughly recommended. Almost without exception the papers are written with directness and clarity, and they form really readable accounts of the investigations that their authors have themselves conducted. The emphasis throughout is on the methods used in the studies but almost all the papers give sufficient of the results obtained to satisfy the appetite they have whetted.

Mental Deficiency. The Changing Outlook. Edited by Ann M. Clarke and A. D. B. Clarke. (Pp. xvi+513; illustrated. 45s.) London: Methuen & Co. Ltd. 1958.

This book, appearing not long after the more clinically orientated work of Hilliard and Kirman, is in many respects the complement of the latter. It is concerned with the psychology rather than the psychiatry of the defective; and with the social factors which influence his development, rather than with his neuropathology. There are a number of contributors, all lay psychologists, and their contributions have been co-ordinated into a readable volume in an unusually felicitous way.

The medical reader may feel that a doctor or two should have been included, and this is especially so in the sections on ætiology and in a short but unmistakably lay account of schizophrenia in childhood. Nevertheless, since psychiatrist and psychologist must collaborate, and since each is the poorer without the assistance the other can give, the book gives a most helpful insight into the knowledge the psychologist possesses and his own special way of expressing it. The account given of the "brain damage" concept, widely misunderstood by psychiatrists and psychologists alike, is notable for its clarity and accuracy.

Perhaps the most attractive feature of the book lies in its hopeful attention to learning, training, social rehabilitation, and even psychotherapy. These things are considered dispassionately and without sentiment, and yet in a way that can only encourage those whose work with defectives may seem at times wasted and pointless. It is a pleasure to recommend what is now the second volume of outstanding merit about mental defectives, and produced within the space of two years.

Studies on Fertility 1958. Including papers read at the Conference of the Society for the Study of Fertility, London, 1958. Being Volume X of the Proceedings of the Society. Edited by R. G. Harrison, M.A., D.M. (Pp. x+176; illustrated. 25s.) Oxford: Blackwell Scientific Publications. 1958.

This tenth volume of Fertility Studies opens with the second Oliver Bird Lecture delivered by Dr. Gregory Pincus in London in April 1958. This paper on oral contraceptives opens a vast new field and gives a preliminary report on the Puerto Rico trial of norethynodrel.

In contrast a later paper by Margaret Jackson gives a critical appraisal of the uses of these new oral progestogens in cases of infertility.

The veterinary papers emphasize the species differences in results and in many cases it is difficult to correlate the findings with human physiology. The effects of varicocele are again recorded, pointing to the necessity for early operation if permanent damage to spermatogenesis is to be prevented. There is also a critical assessment of retrodisplacement by Mr. Fouracre Barns. He concludes that in itself it is neither a cause of infertility nor of abortion. There are in all 9 excellent papers on the male and 7 on the female. A word of caution is perhaps not out of place. The human and animal experiments reported confirm that 19-nor-ethisterone effectively controls fertility; that there is recovery as soon as treatment stops; but it still has to be proved that prolonged exhibition of this drug has no permanent effect on ovarian function.

Major Surgery for Pulmonary Tuberculosis. By R. S. Francis, M.D., M.R.C.P., and M. P. Curwen, M.A. (Pp. x+96; illustrated. 12s. 6d.) London: Staples Press Ltd. 1958.

This is the work of a joint Committee of the British Tuberculosis Association and the Society of Thoracic Surgeons, and is the first of three volumes recording the findings of an enquiry into the immediate and long-term results of major surgery in pulmonary tuberculosis. This Volume, Part I, is concerned with a two-year follow-up of 6,050 patients operated on in the United Kingdom between April 1, 1953, and March 31, 1954, with the exception of certain special groups, including those with bilateral disease, pre-operative fistulæ, and children.

The authors deal, among other matters, with the assessment of clinical material, details of surgical procedures, post-operative complications, major complications and mortality. They draw a comparison between resection and collapse measures. The information has been so well condensed that it is hardly possible to go into detail. It is sufficient to say that this volume, with the two parts which are to follow, makes a valuable contribution to an understanding of the place of surgery in the treatment of this disease, and of the choice of procedure.

Cancer. Edited by Ronald W. Raven, O.B.E. (Mil.), T.D., F.R.C.S. Vol. 5. (Pp. viii+406+19; illustrated. 85s.) London: Butterworth & Co. (Publishers) Ltd. 1959.

This volume is entirely devoted to the radiotherapy of cancer. In contrast to the previous volumes, the contributors all belong to the British School of Radiotherapy, an expression of the standing of the School rather than of medical chauvinism. Just over a third of the volume deals with such general subjects as the physical properties of radiations, the biological basis of radiotherapy, methods of radiation therapy, artificial radio-isotopes in cancer, and radiation protection. The remaining chapters deal with the indications for and details of radiotherapy in cancer of the various regions. The writing is clear and succinct, and there is full recognition of the limitations of radiotherapy. The book will be useful not only to trainees in radiotherapy, but to surgeons who want to know what their radiotherapeutic colleagues can offer in the treatment of cancer and the principles on which they work.

du MAURIER
du MAURIER CIGARETTES
The finest filter tip cigarette
The du Maurier filter tip gives a cool clean smoke with no loose bits in the mouth. The du Maurier blend of tobacco has a fine satisfying flavour. And the smart red box ensures that the last cigarette is as fresh as the first. In fact, you'll like everything about
du MAURIER

PROCEEDINGS PRICE LIST

Copies of the whole *Proceedings* may be purchased through any bookseller or direct from the publishers. Prices are as follows:

Single copies	10s. 6d. each, post free (U.S.A. $2.00).
Annual subscription, covering 12 monthly issues and annual index	£6 6s. 0d. (U.S.A. $19.00).

Distributing Agents: H. K. Lewis & Co. Ltd., 136, Gower Street, London, W.C.1.

In the U.S.A.: Grune & Stratton, Inc., 381, Fourth Avenue, New York 16, N.Y., U.S.A.

Reprints of Sectional parts may be obtained direct from the Honorary Editors, Royal Society of Medicine, 1, Wimpole Street, London, W.1. Prices are as follows:—

Single copies	3s. 6d. each, post free.
Annual subscription	15s. 0d.

Fellows and Members of the Royal Society of Medicine are asked to apply direct to the Honorary Editors, Royal Society of Medicine, 1, Wimpole Street, London, W.1, for any copies of the *Proceedings* they may require, whether whole or Sectional, in addition to those they receive *gratis*. Prices to Fellows and Members are as follows:—

Whole *Proceedings:*

Single copies	7s. 6d. each, post free.
Complete volume (12 monthly issues and annual index)	£5 0s. 0d.

Sectional *Proceedings:*

Single copies	3s. 0d. each, post free.
Annual subscription	10s. 0d.

The perfect drink for every occasion

JOHNNIE WALKER

Fine Old Scotch Whisky

BORN 1820—STILL GOING STRONG

NOTICE TO ADVERTISERS

Applications for advertisement space in the "Proceedings" should be made to:

H. S. JANES & PARTNERS

LIMITED

99 GOWER STREET, LONDON, W.C.1

TELEPHONE: EUSTON 3221

In tune with

NATURE

'ACTIDIL', *most potent of the antihistamines, gives rapid relief of allergies. Young and old patients "out of tune" with nature will be restored by two or three daily doses of* 'ACTIDIL' *Elixir or* 'ACTIDIL' *Tablets.*

'ACTIDIL' BRAND

TRIPROLIDINE HYDROCHLORIDE

BURROUGHS WELLCOME & CO.
(The Wellcome Foundation Ltd.) LONDON

PROCEEDINGS PRICE LIST

Copies of the whole *Proceedings* may be purchased through any bookseller or direct from the publishers. Prices are as follows:

Single copies	10s. 6d. each, post free (U.S.A. $2.00).
Annual subscription, covering 12 monthly issues and annual index	£6 6s. 0d. ($19.00).

Distributing Agents: H. K. Lewis & Co. Ltd., 136, Gower Street, London, W.C.1.

In the U.S.A.: Grune & Stratton, Inc., 381, Fourth Avenue, New York 16, N.Y., U.S.A.

Reprints of Sectional parts may be obtained direct from the Honorary Editors, Royal Society of Medicine, 1, Wimpole Street, London, W.1. Prices are as follows:—

Single copies	3s. 6d. each, post free.
Annual subscription	15s. 0d.

Fellows and Members of the Royal Society of Medicine are asked to apply direct to the Honorary Editors, Royal Society of Medicine, 1, Wimpole Street, London, W.1, for any copies of the *Proceedings* they may require, whether whole or Sectional, in addition to those they receive *gratis*. Prices to Fellows and Members are as follows:—

Whole *Proceedings:*

Single copies	7s. 6d. each, post free.
Complete volume (12 monthly issues and annual index)	£5 0s. 0d.

Sectional *Proceedings:*

Single copies	3s. 0d. each, post free.
Annual subscription	10s. 0d.

The perfect drink for every occasion

JOHNNIE WALKER

Fine Old Scotch Whisky

BORN 1820—STILL GOING STRONG

NOTICE TO ADVERTISERS

Applications for advertisement space in the "Proceedings" should be made to:

H. S. JANES & PARTNERS

LIMITED

99 GOWER STREET, LONDON, W.C.1

TELEPHONE: EUSTON 3221

In tune with

NATURE

'ACTIDIL', *most potent of the antihistamines, gives rapid relief of allergies. Young and old patients "out of tune" with nature will be restored by two or three daily doses of* 'ACTIDIL' *Elixir or* 'ACTIDIL' *Tablets.*

'ACTIDIL' BRAND

TRIPROLIDINE HYDROCHLORIDE

BURROUGHS WELLCOME & CO.
(The Wellcome Foundation Ltd.) LONDON

In all œdematous conditions

HYDRENOX

HYDROFLUMETHIAZIDE

ORAL DIURETIC

offers the following important advantages:-

Hydrenox is at least ten times as potent as chlorothiazide.

The cost of treatment with Hydrenox is lower than with any other potent oral diuretic.

In many cases a single daily dose produces an adequate response.

PACK AND PRICE

Each tablet contains 50 mg. of hydroflumethiazide. Available in containers of 100 and 500 tablets. Basic N.H.S. price 24/- and 116/- (plus P. Tax) respectively. Normal dosage 1-4 tablets daily.

Literature and further information gladly sent on request

BOOTS PURE DRUG COMPANY LIMITED, NOTTINGHAM, ENGLAND

Printed in England by Staples Printers Limited, at their Great Titchfield Street, London, establishment.